

THE IMPACT OF MARKET STRUCTURE ON ONCOLOGY CARE

Aaron Nicholas Winn

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Health Policy & Management in the Gillings School of Global Public Health.

Chapel Hill
2017

Approved by:

Stacie Dusetzina

Ethan Basch

George Mark Holmes

Nancy Keating

Justin Trogon

© 2017
Aaron Nicholas Winn
ALL RIGHTS RESERVED

ABSTRACT

Aaron Nicholas Winn: The Impact of Market Structure on Oncology Care
(Under the direction of Stacie Dusetzina)

The market structure of oncology care is undergoing dramatic consolidation. Little work has examined how market structure impacts oncology care. This study has three objectives: (1) investigate the effect of market structure on geographic access to care for patients receiving infused chemotherapy; (2) investigate the impact of market structure on Medicare reimbursement for patients receiving infused chemotherapy; and (3) evaluate how the market structure impacts the speed of diffusion in the use of new high- and low-value treatments for patients.

Using a 20% sample of Medicare Fee-For-Service claims from 2008 to 2014, we identified a cohort of 142,770 patients receiving infused chemotherapy for cancer and 89,096 new users of chemotherapy. We assessed relationships between 1) competition and the number of chemotherapy-administering physicians within 25, 50, and 75 miles of the patient's zip code and the distance traveled to receive chemotherapy, 2) competition and Medicare expenditures for infused chemotherapy, and 3) competition and diffusion of new treatments.

We find that a one standard deviation increase in logged Herfindahl-Hirschman Index (HHI) (i.e., market becoming less competitive) increases the average distance traveled from 100 to 112 miles and decreases the average number of physicians within 75 miles from 346 to 312 physicians. When examining spending, we find that spending decreases as markets become less competitive at the claim service-line level and the day level but is not impacted when looking at total spending in the six months following treatment initiation. Finally, we examined five newly approved medications or existing medications with new indications: (nab-paclitaxel, bendamustine, degarelix, temsirolimus, and bevacizumab) and find that the impact of competition on the diffusion of a new treatment varies by treatment. Nab-paclitaxel, a lower value drug, diffuses slower as markets become less competitive, whereas bendamustine, a higher value

drug, diffuses faster as markets become less competitive. We do not find significant associations between market competition and drug diffusion for the other drugs studied.

Competition impacts patients' geographic access to care. The association between competition and healthcare spending and diffusion of medications is not consistent. Future research should examine how competition impacts patients' access to care in other clinical areas, drivers for increased spending in consolidated areas, and the quality of care is impacted by competition for cancer patients.

TABLE OF CONTENTS

LIST OF TABLES	viii
LIST OF FIGURES	ix
CHAPTER 1. OVERVIEW	1
Specific Aims	1
Executive Summary.....	2
CHAPTER 2. STUDY RATIONALE	6
Background.....	6
Consolidation in the Healthcare Marketplace	6
Competition and Access to Care for Cancer Patients (Aim 1).....	6
Competition and Medicare Spending on Health Services Received by Patients with Cancer (Aim 2).....	7
Changes the Diffusion of High- and Low-Value Chemotherapies and the Impact of Competition (Aim 3)	8
Study Rationale	8
CHAPTER 3. METHODS	10
Overview	10
Conceptual Model.....	10
Data	11
Sample.....	12
Key Variables.....	13
Analytic Approach.....	16
Aim 1. To Assess the Effect of Consolidation on Access to Chemotherapy for Patients with Cancer	16
Aim 2. To Examine the Effect of Cancer Care Consolidation on Medicare Spending for Infused Chemotherapy and Overall Spending	17
Aim 3. To Examine the Effect of Cancer Care Consolidation on Use of New High- and Low-Value Treatments	17

CHAPTER 4. INVESTIGATING THE ASSOCIATION BETWEEN COMPETITION AND GEOGRAPHIC ACCESS TO CHEMOTHERAPY AMONG CHEMOTHERAPY USERS	20
Introduction	20
Methods	21
Data	21
Statistical Analysis	24
Results	24
Distance Traveled	25
Distance Traveled Sensitivity Analysis	25
Number of Physicians Providing Chemotherapy	25
Number of Physicians Providing Chemotherapy Sensitivity Analysis	26
Discussion	26
CHAPTER 5. EXAMINING THE ASSOCIATION BETWEEN COMPETITION AND SPENDING FOR MEDICARE CANCER PATIENTS.....	32
Introduction	32
Methods	33
Sample	33
Variables	33
Statistical Analysis	36
Results	36
Discussion	37
CHAPTER 6. IMPACT OF COMPETITION ON THE USE OF NEW HIGH AND LOW VALUE CHEMOTHERAPY AGENTS.....	41
Introduction	41
Methods	42
Data	42
Sample and Outcome	42
Exposure	43
Covariates	43
Statistical Analysis	44
Sensitivity Analysis.....	45

Results.....	45
Diffusion of Medication:.....	45
Discussion	47
CHAPTER 7. DISCUSSION	54
Conclusions	54
Competition and Access to Chemotherapy	54
Competition and Spending.....	55
Competition, Value, and the Diffusion of New Treatments	56
Clinical and Policy Implications	57
Limitations.....	58
Future Directions	59
REFERENCES	60

LIST OF TABLES

Table 4.1. Sample Characteristic of Fee-for-Service Medicare Cancer Patients Using Chemotherapy Between 2008 and 2014.....	29
Table 4.2. Coefficients of the Association of Log HHI to Distance Traveled to Care	30
Table 4.3. Coefficients of the Association of Log HHI to Number of Chemotherapy Administering Physicians	30
Table 4.4. Adjusted Risk Ratios of the Association of Log HHI to Number of Chemotherapy Administering Physicians Within 50 and 25 Miles	31
Table 5.1. Sample Characteristic of Fee-for-Service Medicare Beneficiaries Using Chemotherapy Between 2008 and 2014.....	39
Table 6.1. Sample Characteristics of Fee-For-Service Medicare Beneficiaries Between 2008 and 2014.....	49
Table 6.2. Adjusted Risk Ratios Showing the Association Between Competition Quartiles and the Use of New Medications	51
Table 6.3. Adjusted Risk Ratios Showing the Association Between Competition Quartiles and the Diffusion of Bevacizumab	53

LIST OF FIGURES

Figure 3.1. The Relationship Between the Market Structure and Cost, Quality, and Access	19
Figure 5.1. Predicted Health Care Spending by HHI Quartile	40
Figure 6.1. Diffusion of New Treatments Over Time	50
Figure 6.2. Predicted Probabilities for the Diffusion of New Treatments with Statistically Significant Associations with HHI Quartile	52

CHAPTER 1. OVERVIEW

Specific Aims

Hospital mergers and acquisitions have dramatically increased since 2010 and are projected to continue to increase in the coming years [1]. By merging with other hospitals and buying physician practices, expanding hospitals are improving their market advantage by decreasing competition [2]. Hospital mergers and acquisitions have uniquely affected cancer care. Since 2006, 35% of community oncology clinics have merged or entered into a financial relationship with a hospital [3]. As a result, more chemotherapy is received in hospital outpatient settings rather than physician offices [4]. This shift in site of care (i.e., moving from office-based to outpatient) can result in Medicare paying more for the same service [5]. In 2005, 13.5% of chemotherapy was delivered in a hospital setting versus 33% in 2013 [3]. Despite this substantial change, little to no research has examined how cancer care consolidation has impacted cost, quality, and access to care for patients. Previous research on healthcare market competition in various settings has found an association between reduced competition, increased prices, and reduced quality of care [6–8]. Additionally, understanding how competition impacts patient geographic access to care is an understudied area [9].

The long-term goal of this research is to understand how hospital mergers and acquisitions impact cancer care and costs. The objective of this study is to understand how consolidation of cancer care is associated with access, cost, and quality for patients with cancer. The central hypothesis is that cancer care consolidation results in reduced geographic access for patients, increased Medicare spending, and improved quality of care. The rationale for this study is that the organization of hospital systems and cancer care is rapidly changing, yet little attention has been focused on how these changes impact patient care and healthcare costs. As competition decreases, I hypothesize that: (1) patient access to care will decrease because chemotherapy services will be provided at fewer locations with differential effects based on

geographic area; (2) spending will increase due to shifting the site of care from physician offices to the outpatient hospital setting; and (3) treatments will diffuse faster in consolidated markets because larger organizations have more standardized treatment protocols. Understanding how hospital and provider consolidation impacts oncology access, costs, and quality will be important to inform the future regulation of healthcare markets.

Aim 1: To assess the effect of consolidation on access to chemotherapy for patients with cancer.

Hypothesis: Consolidation will reduce the number of providers that are in close geographic proximity (< 75 miles) to patients and increase distance traveled for patients living outside of large urban areas.

Aim 2: To examine the effect of cancer care consolidation on Medicare spending for infused chemotherapy and overall spending.

Hypothesis: Consolidation will be positively associated with Medicare spending for infused chemotherapy as well as overall spending.

Aim 3: To examine the effect of cancer care consolidation on the use of new high- and low-value treatments.

Hypothesis: Hospital consolidation will be associated with increased use of high-value services and decreased use of low-value drugs.

The implications of these findings are significant. Currently, the benefits of consolidation are being debated by academics and government officials [1, 10, 11]. This study can directly inform policymakers as to whether cancer care consolidation affects access to chemotherapy, increases the spending for chemotherapy for patients with cancer, and affects diffusion of new treatments.

Executive Summary

Mirroring changes happening in the broader healthcare marketplace, the organization of cancer care is changing, with hospitals merging (horizontal integration) and hospitals acquiring physician practices (vertical integration) [12]. Recent research has found that there has been substantial vertical integration in recent years, which has resulted in a doubling of the proportion

of hospital-owned practices (from 30% of all practices in 2004 to close to 60% in 2015) [12].

There is debate within the health policy community on the impact of consolidation. Supporters argue that consolidation will result in improved care coordination for patients and improve the quality of care while others believe this may limit patient choice and reduce care quality due to reduced competitive pressures [13].

There has been limited empirical research to examine how the recent wave of consolidation impacts patients. The existing literature focused on spending for commercially insured patients, finding that reduced competition increases spending [6, 14]. This body of work has not examined whether competition is associated with geographic access to care for patients, the impact on spending for Medicare patients, and the quality of care provided.

This study contributes to the cancer health services literature by assessing the impact of competition on cancer care. This dissertation has three objectives: 1) to assess the relationship between competition and geographic access to care; 2) to assess the relationship between competition spending; and 3) to examine if consolidation impacts the rates of adoption of new medications in relation to their estimated value.

To achieve these objectives, we used generalized linear model with the appropriate link and distribution to assess the relationships between 1) competition and distance travelled to chemotherapy and the number of physicians providing chemotherapy geographically close, 2) competition and spending for chemotherapy at the claim-line, day of service, and total spending for a treatment episode level (six months after initiating chemotherapy), and 3) competition on the diffusion of new chemotherapy agents and explore if value impacts the relationship. For Aims 1 and 2 we include market-level fixed effect to control for time invariant observable and unobservable factors that may be associated with the geographic distribution of care and reimbursement for services. Additionally, in Aim 2 we include fixed effects for each drug administered to control for spending differences that could be driven by the drug administered.

In Aim 1, we found that a one standard deviation increase in log HHI (i.e., a market is less competitive) increases the average distance traveled from 100 to 112 miles (coefficient=0.07; 95% CI=0.06, 0.07) and decreases the average number of physicians within 75

miles from 346 to 312 (coefficient = -0.09; 95% CI= -0.10, -0.07). Furthermore, when models are stratified by urbanicity, we found that the association is larger in urban over non-urban areas for distance traveled (urban areas, coefficient =0.26, 95% CI=0.25, 0.27; non-urban areas, coefficient =0.05, 95% CI=0.04, 0.05) and number of providers (urban areas, coefficient =-0.16, 95% CI=-0.19, -0.13; non-urban areas, coefficient =-0.07, 95% CI=-0.09, -0.05).

These findings suggest that a patient's geographic access to care decreases as markets become less competitive. This finding is particularly important for chemotherapy, because patients need to repeatedly travel to facilities to receive infused chemotherapy and prior work has found that travel distance can result in reduced adherence to chemotherapy regimens [15]. Additionally this finding is notable because, to our knowledge, it is the first study to examine how geographic access to care is impacted by market competition.

In Aim 2, we found that a one standard deviation increase in log HHI (i.e., a market is less competitive) decreased line-item claim-level spending by 1.58 percentage points (coefficient = -0.07; 95% CI=-0.10, -0.03) and decreased day of service spending by 1.02 percentage points (coefficient=-0.04; 95% CI=-0.07, -0.01) but was not associated with six month total episode-based spending (coefficient =0.04; 95% CI= -0.01, 0.09).

This finding was counter to our hypothesis that as a market grew more concentrated spending would increase. Because we controlled for drug received, differences in specific drugs used between settings are likely not driving this counterintuitive result. Our empirical results show oncology care consolidation only slightly impacted spending at the claim or day level but did not impact overall spending.

Findings from this study suggest that decisions to consolidate were not driven by being able to bill Medicare at higher rates. Rather, consolidation may be driven by other reimbursement-related factors such as the 340B program, which allows most hospitals to buy chemotherapy drugs at deeply discounted rates. However, recent studies have found that the 340B program was not associated with hospitals buying community practices [12]. Therefore, if hospitals are not purchasing community oncologists to benefit from the 340B program, this fact along with findings from the current study suggest that vertical integration decisions may have

been driven by other factors. These factors could be related to payment reform such as Accountable Care Organizations (ACOs) and bundled payments from Medicare. Other factors could include favorable reimbursement from private insurers or private insurers increasing use of narrow networks [12].

Finally, in Aim 3, we hypothesized that reduced competition would be associated with faster diffusion of high-value drugs and slower diffusion of low-value drugs. We examined five newly approved medications or existing medications with new indications approved (paclitaxel, bendamustine, degarelix, temsirolimus, and bevacizumab) and found that the impact on the diffusion varies by treatment. Nanoparticle albumin-bound (nab)-paclitaxel, a low-value drug, diffuses slower as markets become less competitive whereas bendamustine, a high-value drug, diffuses faster as markets become less competitive. For bevacizumab, degarelix, and temsirolimus—a low-, moderate-, and high-value drug, respectively—we do not find significant associations between market competition and drug diffusion.

This study found mixed evidence on the influence of competition on the diffusion of new medications. Paclitaxel, a low-value drug, was used less in less competitive markets whereas the high-value bendamustine was used more in less competitive areas. Looking at these two medications, it may suggest that there is greater centralized control in consolidated markets, which encourages use of high-value medications. However, given the small number of drugs examined and inconsistent findings across studied treatment the findings should be interpreted with caution. Additional research should be done to examine if this finding is consistent for other medications and in other clinical areas.

CHAPTER 2. STUDY RATIONALE

Background

Consolidation in the Healthcare Marketplace

There has been a dramatic increase in hospital mergers and acquisitions since 2008 and this trend is predicted to continue, with one-fifth of hospitals forecasted to merge within the next five years [1, 16]. A recent study found that over 250 mergers and acquisitions occurred in 2013 [16]. Hospital mergers are expected to improve hospitals' financial performance by allowing them to negotiate for higher prices from private payers and by improving efficiency. Prior work has found that mergers can result in cost-savings for hospitals generated from a combination of increased efficiency due to economies of scale and more generous reimbursements from private payers [17–19]. If providers and hospitals spend these profits on the services they provide, consolidated hospitals could improve the quality of care they deliver. Furthermore, the quality of care for procedures could improve where there is a strong relationship between volume and outcomes, such as surgical outcomes for cancer patient [20]. Despite significant recent changes in the structure of the oncology market via hospital consolidation, there has been little work to evaluate its impact on patients. The goals of the proposed study are to provide policymakers and stakeholders with evidence that can be applied to inform potential regulation of healthcare markets and to describe the relationship between oncology market structure access to, quality of, and costs of cancer care.

Competition and Access to Care for Cancer Patients (Aim 1)

Although the research base on the geographic distribution of chemotherapy providers is limited, a consistent finding is that there are significant geographic disparities in access to cancer care [21–23]. Most of the prior research in this area uses data that are over a decade old and do not capture recent changes in market structure. A more recent study using data from the late 2000s found that there were significant geographic disparities in access to care for colorectal

cancer patients needing chemotherapy. Specifically, geographic disparities in access to care impacted the use of chemotherapy because people with increased travel times were less likely to use chemotherapy [15]. Although this work establishes a foundation for research on the impact of geographic care disparities, gaps remain on the role that market structure plays in the geographic distribution of care. For example, hospitals can buy private oncology practices and keep the facilities open or they can consolidate cancer services at central locations.

The proposed analysis for Aim 1 of this dissertation will contribute to the existing literature by examining how changes in market structure have impacted geographic access to care for patients receiving infused chemotherapy. Further, this study may shed light on the impact of market structure on access to care more broadly, such as dialysis services, an area of research that is historically limited.

Competition and Medicare Spending on Health Services Received by Patients with Cancer (Aim 2)

Since 2008, roughly 700 private oncology practices have been bought by hospitals, resulting in more patients being seen in hospital outpatient departments and fewer patients seen in physician offices [4, 16, 24]. From 2008 to 2012, the amount of chemotherapy provided in hospital outpatient departments has increased by over 60% [24, 25]. This shift in delivering chemotherapy infusions within the outpatient rather than an office-based setting is expected to increase healthcare spending per infusion because Medicare reimburses hospital outpatient services at a higher rate than physician offices. This may result in increased spending for infused chemotherapy as well increased overall spending. Industry reports suggest that the costs a Medicare patient incurs for being treated at a hospital outpatient department are 13% to 20% higher when compared to treatment received at a physician's office [4, 24, 25]. These prior analyses may be biased, however, because they do not fully account for observable differences in patient populations and unobservable differences in markets, both of which affect the cost of care provided to patients.

Changes the Diffusion of High- and Low-Value Chemotherapies and the Impact of Competition (Aim 3)

Little research has explored how market structure impacts cancer care [26], or the influence of market structure on health service delivery more broadly. Although there is a body of literature that finds increased competition increases quality for Medicare beneficiaries [7], there is little research that examines the diffusion of new treatments or medication by market structure. The small body of literature across clinical areas finds that market structure does impact the diffusion of a new treatment and that competition is associated with faster rates of diffusion due to competitive pressures, but this body of work has not examined how value impacts diffusion [27–31]. However, there is an argument in favor for hospital consolidation that theorizes that the quality of care will improve because larger organizations will be able to implement system-wide quality control, however this claim has not been tested [1].

Study Rationale

Substantial debate exists within the oncology community on how to best improve the value of care provided with much of the debate focused on the rising costs of new drugs [32]. However, many system-level factors have been, so far, under-researched, including that of whether provider market structure impacts the access to, costs of, and quality of care provided. This study is innovative in its use of rigorous methods to examine how the changing market structures due to acquisitions, mergers, and consolidations impact access to, costs of, and quality of cancer care.

Although industry reports have found that the amount of chemotherapy received in a hospital has more than doubled in the past 10 years [3], this finding has not been confirmed from other studies and no work has examined factors associated with this change. And although there is a substantial body of work related to how Medicare spending is impacted by the site of care for services (i.e., hospital outpatient or physician office) [33] and it is believed that cancer care consolidation will result in increased hospital outpatient-based care [3], to date there are no empirical studies to test if this is true. This study will directly test if consolidation is changing cancer care spending.

The role that the provider market structure plays in geographic access to care for patients is unknown. Recent work has found that distance to care impacts patients' use of chemotherapy, but no work has examined factors that are contributing to changes in geographic access [15]. This study will provide new knowledge about how a changing provider marketplace influences geographic access to care.

This project will also generate new knowledge on the role of the provider market structure in the diffusion of new treatments where there has been little research in context of cancer [26] or in other clinical areas [27, 29, 30]. Furthermore this study is unique in examining the value of the treatment that has previously been ignored. This study will examine how market structure impacts the diffusion of a treatment and if the value of a treatment modifies patterns of diffusion.

CHAPTER 3. METHODS

Overview

The goal of this study is to determine the effect of competition on access, Medicare spending, and quality for patients with cancer. However, the main exposure of interest, market competition, may be endogenous. For example, high-quality hospitals may have better financial performance and thus may capture a larger market share. To address this potential problem, we created an exogenous measure of competition based on variation in the distance between patients and providers, which allows us to find a causal relationship between market structure and outcomes. The study will use a 20% random sample of fee-for-service Medicare claims from 2007 to 2014. We will include patients that receive infused chemotherapy for a cancer-related indication between 2008 and 2014. Aim 1 will explore how consolidation impacts patient geographic access to chemotherapy providers. Aim 2 will explore the relationship between consolidation and Medicare expenditures. Aim 3 will examine if consolidation impacts the rates of adoption of new medications in relation to their estimated value.

Conceptual Model

A conceptual model was developed for this study that highlights the relationship between provider competition and access to care, spending, and quality of care (see Figure 3.1). This model depicts the interrelatedness of market structure to other outcomes. The solid lines between factors show the relationships the study will investigate while the dashed lines show relationships that are believed to exist but are sources of endogeneity. This model illustrates that the market structure directly impacts quality of care, site of care, and access to care. The model then shows that the site of care will directly impact the amount of Medicare expenditures for services and that the quality of care could influence the market structure, potentially due to higher quality providers attracting more patients. Additionally, it is expected that there is a relationship between increased Medicare expenditures and quality of care if hospitals take the additional revenue and invest it

into their cancer services. This would then likely improve quality of care, which could again impact the overall market structure. We operationalize each aim as described below:

Aim 1 assesses how market structure changes could impact the geographic location of providers in relation to patients. We hypothesize that as providers are consolidated within hospital systems and the marketplace becomes less competitive, there will be fewer locations offering infused chemotherapy, which will reduce geographic access to cancer care for patients and result in longer travel times. We will examine if this result is consistent across urban (county population 1 million or more) and non-urban areas.

Aim 2 examines how market structure impacts the site in which care is delivered (i.e., physician's office or hospital outpatient setting) and how this ultimately may change Medicare expenditures.

Aim 3 explores the relationship between market structure and impact on the delivery of high-value care. For this Aim, we use the diffusion of new medications of higher versus lower value.

Data

The data for this study were obtained using the 20% random sample of the Medicare Standard Analytic Files, which includes all Medicare fee-for-service beneficiaries. We identified a prevalence cohort of cancer patients that used infused chemotherapy between 2008 and 2014. Using the Agency for Healthcare Research and Quality's (AHRQ) hierarchical clinical classification (HCC) software we identified claims as being cancer-related based on the International Classification of Disease version 9 (ICD-9) codes [34]. Chemotherapy use will be identified by Healthcare Common Procedure Coding System (HCPCS) J9XXX codes.

To identify markets for chemotherapy, we examined all of the chemotherapy provided within a market and assigned each chemotherapy claim to a practice. A practice can be a physician practice, hospital, or even an individual physician; we define a practice based on the tax identification number (TIN) included on the submitted claim. Use of chemotherapy was measured using Medicare Part B claims for outpatient and physician services. For chemotherapy delivered in non-hospital-affiliated outpatient settings, the physician practice (i.e., the firm) was

determined by the TIN, which was recorded on the claims. Additionally, the location of where the service was provided is recorded on the claim for non-hospital–affiliated outpatient claims. For chemotherapy provided in hospital-affiliated outpatient settings, the TIN and location of the TIN are not directly provided on the claim but the national physician identifier (NPI) is available. Using the NPI and the Medicare Data on Provider Practice and Specialty (MD-PPAS) and National Plan and Provider Enumeration System (NPPES), we linked NPI to a TIN using MD-PPAS and practice zip code using NPPES to determine the location and practice information for an encounter. If a physician is associated with more than one TIN, we selected the TIN with the largest percentage of total claims submitted to Medicare.

We included patient demographic and enrollment information from the Medicare Beneficiary Summary File, which includes demographic and enrollment information about patients and zip code of residence. We used the U.S. Census Tiger files to identify the latitude and longitude coordinates for each zip code centroid [35].

Sample

We created a prevalence cohort of cancer patients that received physician-administered chemotherapy or hormonal therapy between January 1, 2008, and December 31, 2014. Eligible individuals were enrolled in Medicare Parts A and B when they received chemotherapy. There were 142,770 individuals meeting these criteria and eligible for inclusion in Aim 1. From this sample, we created a new user cohort of cancer patients with who were continuously enrolled in FFS Medicare Parts A and B for six months before and after their first chemotherapy claim, creating a six-month washout period and an analytic sample of 86,039 individuals. These individuals were included in Aim 2. For Aim 3, we subset the Aim 2 cohort to create disease-specific cohorts (breast, lung, chronic lymphocytic leukemia (CLL), kidney, and prostate cancer) and their chemotherapy use (breast N=9,499; lung N=4,645; CLL N=2,194; kidney N=1,002; prostate N=22,810). We categorized drug-indication pairs as high- or low-value based on an assessment from Memorial Sloan Kettering's Drug Abacus, a recently developed tool that describes the value of a treatment based on price, life expectancy, and side-effect profile. The tool and related value assessment is built on recent work by Howard et al [36]. We recognize that

our assignment of value is limited by the lack of rich clinical information that would tell us if the drug is prescribed exactly as indicated by the FDA.

To create measures of competition, we identified all patients who received any chemotherapy administered for an indication of cancer during the study period. For Aim 1, we used this prevalence cohort and estimated the distance a patient traveled from their residence zip code to the zip code of the point-of-service delivery. For Aim 2, we examined spending for new users of chemotherapy. In Aim 3, we examined the proportion of patients receiving a specified new treatment as a proportion of all chemotherapy uses among patients with the cancer of interest. For example, among patients with breast cancer within a month, we divided the number of patients receiving bevacizumab by the total number of individuals who have breast cancer and received any chemotherapy within the month.

Key Variables

The main independent variable in our analysis was the competitiveness of a market. We measured competition based on the Herfindahl-Hirschman Index (HHI) [37]. The HHI measures the market structure by squaring the volume shares of a practice within a market. The HHI can range from 0 to 10,000, where the larger the number, the more concentrated and less competitive the market. An HHI of 1,500 or less is considered a competitive market. Because it is not clear what constitutes a market for cancer care, we constructed markets both at the core-based statistical area (CBSA) and Hospital Referral Region (HRR) level [38]. We used the prevalence cohort of patients and all chemotherapy claims when calculating the HHI to reflect the size of the market. We defined practices based on the TIN listed for the physician administering chemotherapy and their market share as the number of chemotherapy infusions administered by the practice.

Because directly measuring market structure may be influenced by unobservable aspects of quality of care, we created an HHI that aims to minimize this bias using the following steps [37, 39, 40]:

1. Create a choice set for patients that will include all practices (i.e., firms based on unique TINs) within 75 miles of a patient's zip code. In sensitivity analysis, we used 25 or 50 miles to test if the results were sensitive to this assumption.
2. Using this choice set, we estimated a patient choice model. Using a conditional logit model, we modeled patient choice as a function of distance between the patient and practice, distance squared, number of physicians associated with the practice (based on the number billing under the TIN), the total annual charges from the practice, charges squared, and year. This model was run separately for each region (northeast, south, central, and west) to ensure model convergence.
3. We used the estimates from the patient choice model to generate the predicted probability that the patient would use each practice in the patient's choice set. However, the number of physicians and charges of a practice may be associated with the quality of the practice. To overcome this bias, when predicting the probability of seeing a practice we set the number of physicians and charges to the means of that patient's choice set.
4. The predicted probabilities were summed across patients to generate the predicted number of patients that would go to each practice. We calculated the market share for each practice by dividing the number of patients seen at each practice by the number of patients within the market.
5. We then squared each practice's market share and sum the market share across all practices within a market (CBSA or HRR) to generate the level of competition (measured as HHI) for that market.

Because this measure of HHI is purely a function of the geographic distribution of a patient and practices, it does not reflect market share differences due to quality variation across providers. This measure mitigates the causal relationship between market structure and the unobservable aspect of quality of care, which may otherwise bias our results.

For Aims 1 and 2, we used the constructed HHI (described previously) and then log HHI to ensure that small changes in HHI (i.e., a hospital acquiring a community oncologist) and large changes in HHI (i.e., hospitals merging) are captured.

For Aim 3, we did not use the same approach described previously to model HHI. Instead we chose to use the directly measure HHI with all results being interpreted as associations. This allows us to describe how actual market competition was associated with diffusion of medications, which will better describe how competition was associated with the diffusion of a medication. Additionally, this analysis is targeted toward a clinical audience and the interpretation of directly measuring market structure is more accessible to that audience. We segmented the HHI into quartiles and modelled the relationship as a categorical variable to allow for non-parametric relationships between competition and use of new treatments over time.

Patient-level covariates are drawn from the Medicare enrollment and claims files. Using the enrollment file, we measured age, race (white, black, other), gender, year, and an urban indicator (county population > 1 million). For Aims 2 and 3, we measured comorbidities using data contained in the Medicare Parts A and B claims files and the comorbidity index developed by Klabunde and colleagues [41]. For Aims 1 and 2, we included fixed effects for the market area based on the beneficiary's zip code of residence to control for time invariant market factors. For Aim 2, we included fixed effects for the drug used (from the claims files) to ensure that any differences in spending were due to differences in reimbursement levels between markets and not due to differences in the expenditures for the drugs administered.

In Aim 1, the dependent variables were the distance traveled by a patient from their home to their site of cancer treatment and the number of physicians providing chemotherapy close (<75 miles) to a patient. To measure the distance travelled by patients to receive care, we used the patient residence zip code from the enrollment file and the practice zip code derived from the claims or NPPES file to measure the Euclidian distance in miles between centroids. In Aim 2, the dependent variable was total Medicare spending as well as patient liability at the line-item claim, day, and total six-month level (which was recorded in claims). All spending was inflated to 2014 U.S. dollars using the consumer price index (CPI). In Aim 3, the dependent variable was the use

of a new drug among the patient population that could benefit from the treatment (breast/bevacizumab; lung/nab-paclitaxel; CLL/bendamustine; kidney/temsirolimus; prostate/degarelix) as observed from claims.

Analytic Approach

The analytic approach for Aims 1, 2, and 3 is outlined below. Overall, we used two approaches to identify the competitiveness of a market. In Aims 1 and 2, we created competition measures by using a patient choice model, where a patient's preference and likelihood of receiving chemotherapy from a practice were based on the distance between patients and practices. This approach ensures that the competition measures do not suffer from endogeneity. However, in Aim 3, we did not use a patient choice model to create the competition measure but instead directly measured competition. Therefore, this analysis simply describes what has occurred.

Aim 1. To Assess the Effect of Consolidation on Access to Chemotherapy for Patients with Cancer

We examined the relationship between competition with the number of practices within 75 miles of the patient and the distance a patient traveled to receive care. Based on model fit, we used a log link and negative binomial distribution when examining the number of chemotherapy administering physicians and a log link and Poisson distribution when examining the distance traveled to a provider.

Because urban patients are more likely to reside in competitive areas, we ran models that were stratified by urbanicity. Primary models controlled for patients' demographic characteristics and included fixed effects for the market. The market fixed effect provides HHI coefficients that are "within-estimates"—meaning that the HHI coefficient(s) would only be impacted if the competitiveness of a market changes during the study period. These market area fixed effects control for any time invariant factors within a market that could confound the findings. This approach provides the most conservative estimates of the impact of competition. In sensitivity analyses we removed the market area-level fixed effects and instead used a generalized estimating equation (GEE) model to account for the correlated error within a market.

Aim 2. To Examine the Effect of Cancer Care Consolidation on Medicare Spending for Infused Chemotherapy and Overall Spending

We examined the relationship between competition and spending for chemotherapy at the claim-line level, day level, and treatment episode level (six months after treatment initiation). Generalized linear models were used to assess the relationship between competition and Medicare expenditures. We performed modified Park tests to determine the appropriate distribution of the mean-variance relationship. Based on the results of these tests, we used a log link and Poisson distribution. All models controlled for patient characteristics and market area fixed effects (either CBSA or HRR) and fixed effects for the drug administered. The market fixed effect provides HHI coefficients that are “within-estimates” as explained previously. Additionally, using fixed effects for the drug administered ensured that differences seen are not driven by differences in the drugs administered but rather by differences in reimbursements for the same services.

Aim 3. To Examine the Effect of Cancer Care Consolidation on Use of New High- and Low-Value Treatments

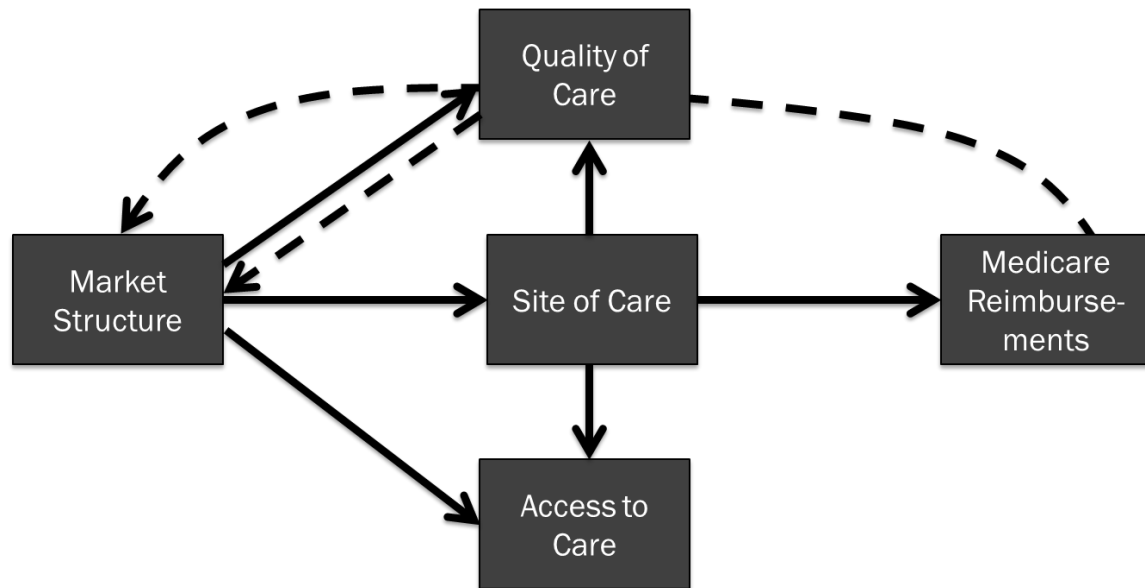
We analyzed the association between competition and diffusion of new medications using a generalized linear model using a log link and binomial distribution and clustered the standard errors at the patient level to account for repeated observations during the analysis period. For each outcome model we included patients’ age, race, gender, Klabunde modification of the Charlson comorbidity score, an urban indicator (county population > 1 million), and time. Time was measured as quarter of calendar year since the FDA approval of the medication. If a unique HCPCS code was not assigned to the treatment when it was approved, we started time once the HCPCS code was approved. Additionally, we ran models with an interaction term for time with HHI quartile to examine if the slope of the diffusion curve varied by quartile.

We altered this approach when examining the diffusion of one medication, bevacizumab. During our study period the FDA indicated that the harms of bevacizumab were likely to outweigh the benefits for patients with breast cancer. To account for this, we use an interrupted time series analysis where we included the previously mentioned covariates and also include a dummy for “time after” and a running variable for the “time since” bevacizumab was reported as being

harmful. We ran models that allowed for interactions of HHI quartiles and the “time after” dummy and the “time since” running variable. Additionally, because bevacizumab was approved for use for other indications before 2008, we included the use of bevacizumab in 2007 within a market (CBSA or HRR) for any cancer to account for prior practice patterns.

We also tested for differences in the diffusion of a medication by value. To do this, we ran a pooled model that included all drugs except bevacizumab. In this model, we included a categorical variable for “value” and interacted value with time to test if high- or low-value drugs diffuse faster or slower. Additionally, we allow for a three-way interaction between value, time, and HHI to examine if the competitiveness of a market impacts diffusion of high- and low-value drugs differently.

Figure 3.1. The Relationship Between the Market Structure and Cost, Quality, and Access



CHAPTER 4. INVESTIGATING THE ASSOCIATION BETWEEN COMPETITION AND GEOGRAPHIC ACCESS TO CHEMOTHERAPY AMONG CHEMOTHERAPY USERS

Introduction

Geographic access to care (in this case, the availability of relevant healthcare providers that are close to a patient) can influence patients' use of and adherence to treatments [21, 23, 42–44]. This is particularly of interest in the area of cancer care because oncologists are not evenly distributed across the country and patients may need to repeatedly travel to oncologists to receive chemotherapy [21, 23, 45]. Prior research has found an association between increased early detection of and survival from cancer and living in areas with an increased availability of physicians [46–48]. Furthermore, increased travel time to providers is associated with a decreased likelihood of having received adjuvant chemotherapy for patients with colorectal cancer or receiving breast-conserving therapy for breast cancer patients [15, 22, 49].

Mirroring changes happening in the broader healthcare marketplace, the organization of cancer care is changing, with hospitals merging (horizontal integration) and hospitals acquiring physician practices (vertical integration) [12]. Recent research has found that there has been substantial vertical integration in recent years with the proportion of hospital-owned oncology practices increasing from less than 30% of practices in 2004 to close to 60% in 2015 [12]. There is debate within the health policy community on the impact of integration. Supporters argue that integration will result in improved care coordination for patients and improve the quality of care while others believe this may limit patient choice and reduce care quality due to reduced competitive pressures [13].

The limited empirical research on the effect of this recent wave of consolidation has focused on spending for commercially insured patients. This body of work has consistently found that spending increases when markets become more consolidated [6, 14]. However, there has been no work to examine whether changes in area-level competition is associated with geographic access to care for patients. Specifically, consolidation could reduce the number of

available providers or the location where the providers practice because merging/acquired practices could remain at their original locations or be moved to a centralized location. This study aims to understand how competition is associated with patients' geographic access to care in two ways: 1) examining the association between market competition and the distance a patient travels to receive care, and 2) examining the association between competition and the number of providers relatively close to a patient.

Methods

Data

We used a random 20% sample of Medicare fee-for-service claims. We created a prevalence cohort of fee-for-service Medicare beneficiaries that received infused chemotherapy at a hospital outpatient department or physician office between 2008 and 2014. To identify a chemotherapy claim, we required that beneficiaries had a cancer-related *International Classification of Disease*, Ninth Edition (ICD-9) code and a Healthcare Common Procedure Coding System (HCPCS) code starting with J9XXX on the same claim. Eligible beneficiaries were enrolled in Medicare Parts A and B when receiving chemotherapy (N=142,770). Our study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

Variables

The primary outcome variables were the distance travelled to receive chemotherapy and the number of physicians providing chemotherapy within 75 miles of a patient with additional sensitivity analysis conducted at the 25- and 50-mile thresholds. We measured the Euclidian distance between the centroid of the patient's zip code and the centroid of the physicians' zip code. We identified the patient's zip code from the enrollment file based on when the patient initiated chemotherapy. To identify the location where chemotherapy was provided we used Medicare Part B claims for outpatient and physician services. For chemotherapy delivered in non-hospital-affiliated outpatient settings, the zip code of the chemotherapy service provider is recorded on the claim. For chemotherapy provided in hospital affiliated outpatient settings, the zip code is not available directly on the claim. Therefore, we identified the performing physician's zip

code by linking the physician's national physician identifier (NPI) to the National Plan and Provider Enumeration System data, which provides the physician's zip code.

The main independent variable in our analysis was competitiveness of the area. We measured competition based on the Herfindahl-Hirschman Index (HHI). The HHI measures the market structure by squaring volume shares of a practice within a market. Because a precise measure of the cancer care market does not yet exist, we constructed markets at the core-based statistical area (CBSA) and Hospital Referral Region (HRR). We used the prevalence cohort of patients and all chemotherapy claims when calculating the HHI to reflect the size of the market. We defined firms (practices) based on the tax identification number (TIN) listed for the physician administering chemotherapy and their market share as the number of chemotherapy infusions administered by the practice. Because the TIN is not provided on outpatient hospital claims, for these providers we used the Medicare Data on Provider Practice and Specialty (MD-PPAS) files to obtain this information. If a physician is associated with more than one TIN, we selected the TIN with the largest percentage of total claims submitted to Medicare. However for all non-hospital-affiliated claims, the TIN is provided and we do not need to link to MD-PPAS to assign physicians to a practice.

Because directly measuring market structure may be influenced by unobservable aspects of quality of care, we created an HHI that aims to minimize this bias using the following steps [37, 39, 40]:

1. Create a choice set for patients that will include all practices (i.e., practices) within 75 miles of a patient's zip code. In sensitivity analysis, we used 25 or 50 miles to test if the results were sensitive to this assumption.
2. Using this choice set, we estimated a patient choice model. Using a conditional logit model, we modeled patient choice as a function of distance between the patient and practice, distance squared, number of physicians associated with the practice (based on the number billing under the TIN), the total annual charges from the practice, charges squared, and year. This

model was run separately for each region (northeast, south, central, and west) to ensure model convergence.

3. We used the estimates from the patient choice model to generate the predicted probability that the patient would use each practice in the patient's choice set. However, the number of physicians and charges of a practice may be associated with the quality of the practice. To overcome this bias, when predicting the probability of seeing a practice we set the number of physicians and charges to the means of that patient's choice set.
4. The predicted probabilities were summed across patients to generate the predicted number of patients that would go to each practice. We calculated the market share for each practice by dividing the number of patients seen at each practice by the number of patients within the market.
5. We then squared each practice's market share and sum the market share across all practices within a market (CBSA or HRR) to generate the level of competition (measured as HHI) for that market.

Because this measure of HHI is purely a function of the geographic distribution of a patient and practices, it does not reflect market share differences due to quality variation across providers. This measure mitigates the causal relationship between market structure and unobservable aspect of quality of care, which may otherwise bias our results.

The HHI can range from 0 to 10,000, where the larger the number, the more concentrated and less competitive the market. An HHI of 1,500 or less is considered a competitive market. We log HHI which ensures that both small (i.e., a hospital acquiring a community oncologist) and large (i.e., hospitals merging) changes in HHI will be captured.

For each outcome model we included patients' age, race (black, white, other), gender, year, and an urban indicator (county population > 1 million). Because urban patients are more likely to reside in a competitive area, we also ran models that were stratified by urbanicity.

Statistical Analysis

Generalized linear models were used to assess the relationship between competition and the number of chemotherapy providers and the distance travelled to a provider, controlling for patient characteristics and market area fixed effects (either CBSA or HRR). The market fixed effect provides HHI coefficients that are “within-estimates”—meaning that the HHI coefficient will only be impacted if the competitiveness of a market changes during the study period. These market area fixed effect control for any time invariant factors within a market that could confound the findings. This will provide us with the most conservative estimate of the impact of competition. In sensitivity analysis we remove the area-level fixed effects and instead used a generalized estimating equation (GEE) model to account for the correlated error within a market.

We used a negative binomial model for estimating the number of chemotherapy-administering physicians available within a 75-mile radius from the patient’s zip code. We conducted sensitivity analysis where the outcome was modified to look at the number of chemotherapy administering physicians within 25 or 50 miles. We used a log link and Poisson distribution for estimating the distance travelled by each patient who received chemotherapy. The model distributions were selected based on model fit as measured by the Akaike Information Criteria and Bayesian Information Criteria [50].

Results

Characteristics of the 142,770 individuals receiving infused chemotherapy included in our cohort are presented in Table 4.1. The mean age of patients was 75 (Standard Deviation (SD): 7), which was similar between urban and non-urban patients. The majority of the population was white (84%), however there were more black patients in urban areas when compared to non-urban areas (11% vs 7%; $P < 0.01$). Overall, most patients resided in competitive areas, with HHI under 1,500. However, urban areas were more competitive than non-urban areas. On average, there were 398 (SD: 452) physicians that provide chemotherapy to Medicare patients within a 75-mile radius of a patient’s zip code. There were fewer chemotherapy physicians for non-urban patients when compared to urban patients (non-urban=188, SD:243; urban =566, SD: 507). The mean distance patients traveled for chemotherapy was 100 miles (SD: 252), however the

distribution of miles traveled was quite skewed—three-quarters of patients travel 29 or fewer miles for chemotherapy.

Distance Traveled

When considering the role of market competition on the distance traveled for chemotherapy (Table 4.2), we found that a one standard deviation increase in log HHI (i.e., a market is less competitive) increases the average distance travelled from 100 to 112 miles when markets are created at the CBSA-level (coefficient=0.07; 95% CI=0.06-0.07). The association is larger when measuring markets at the HRR level (coefficient=0.14; 95% CI=0.13-0.14). Furthermore, when models are stratified by urbanicity, we found that the association is larger in urban over non-urban areas when markets were constructed at the CBSA level (urban areas, coefficient =0.26, 95% CI=0.25-0.27; non-urban areas, coefficient =0.05, 95% CI=0.04-0.05) and at the HRR level (urban areas, coefficient =0.26, 95% CI=0.25-0.27; non-urban areas, coefficient =0.10, 95% CI=0.10-0.11).

Distance Traveled Sensitivity Analysis

Analyses using GEE models found that increased market concentration was associated with increased distance travelled (Table 4.2). These results were consistent across models. However, the effect estimates were larger overall and in non-urban areas when compared to results from the fixed effect models, and the estimates were less precise. Additionally, in the GEE models we did not observe significant heterogeneity on the impact of competition between urban and non-urban areas. This sensitivity analysis confirms the primary analysis and demonstrates that the main finding is not impacted by modelling assumptions.

Number of Physicians Providing Chemotherapy

When looking at the association between market competition and the number of physicians that provide chemotherapy (Table 4.3), we found that a one standard deviation increase in log HHI (i.e., a market is less competitive) decreases the average number of physicians within 75 miles from 346 to 312 at the CBSA-level (coefficient = -0.09; 95% CI= -0.10 - -0.07). The association is larger when measuring markets at the HRR level (coefficient = -0.17; 95% CI= -0.19 - -0.15). When models are stratified by urbanicity, we found that the result was

larger in urban compared to non-urban areas when measuring markets at the CBSA-level (urban areas, coefficient =-0.16, 95% CI=-0.19 - -0.13; non-urban areas, coefficient =-0.07, 95% CI=-0.09 - -0.05), but not when measuring markets at the HRR level (urban areas, coefficient =-0.18, 95% CI=-0.21 - -0.15; non-urban areas, coefficient =-0.17, 95% CI=-0.19 - -0.14).

Number of Physicians Providing Chemotherapy Sensitivity Analysis

We conducted two sets of sensitivity analyses: 1) calculating the number of physicians providing chemotherapy within 25 or 50 miles rather than 75 miles (Table 4.4), and 2) conducting analyses using a GEE model instead of a fixed effects model (Table 4.4). When varying the distance for the number of physicians, we find consistent but slightly larger results. For example, we find that a one standard deviation increase in log HHI decreases the average number of physicians within 25 miles from 100 to 81 physicians at the CBSA-level (coefficient=-0.17; 95% CI=-0.20 - -0.15). When using GEE models, we also found consistent but larger associations (coefficient=-0.84; 95% CI=-0.92 - -0.76). The GEE models did not observe significant heterogeneity between urban and non-urban areas. Again, these sensitivity analyses confirms the primary analysis and demonstrates that the main finding, decreasing competition is associated fewer physicians near a patient, is not impacted by modelling assumptions.

Discussion

Although prior work has documented the impact of geographic access to care for cancer patients, little if any work has explored structural mechanisms and their contributions to the geographic distribution of practices. In this study we aimed to explore the relationship between market competition among oncology providers and patients' geographic access to care. First, we found that most fee-for-service Medicare patients do not travel far for chemotherapy. We observe that 50% of patients travel 12 or fewer miles to receive chemotherapy, with similar median distances travelled between urban and non-urban patients (11 and 15 miles, respectively). However, the top quartile of urban patients travels 23 or more miles while non-urban patients travel 41 miles or more. These results are consistent with prior studies, which find that 54% of Stage III colorectal patients travel 12.5 miles or less for adjuvant chemotherapy [15]. Additionally,

when examining the number of physicians that provides chemotherapy, we find that non-urban patients have fewer providers with a mean of only 28 providers within 25 miles.

We find that increases in market concentration reduce geographic access to chemotherapy for chemotherapy users. Our first finding from the adjusted analysis is that markets become less competitive as the distance travelled to chemotherapy increases. Our second finding from the adjusted analysis exploring patient choice found reduced competition is associated with fewer physicians close to patients. We test this finding using a variety of sensitivity analyses and find consistent results. These findings suggest that a patient's geographic access to care decreases as markets become less competitive.

Our finding is consistent with news reports where hospital executives justify mergers stating that they will “eliminate duplication—for example by consolidating cardiac care or cancer treatment at one site” [10]. This argument states consolidation, and the resulting reduced competition, is justified because chemotherapy will be provided at one site, which will increase efficiencies and likely reduce costs for the hospital. However, this argument ignores how geographic access will be reduced. This finding is particularly important for chemotherapy services because patients need to repeatedly travel to facilities to receive infused chemotherapy and prior work has found that travel distance can result in reduced adherence to chemotherapy regimens [15]. Additionally this finding is significant because, to our knowledge, it is the first study to examine how geographic access to care is impacted by market competition.

Our study had several limitations. First, we only examined fee-for-service Medicare beneficiaries. It is unknown whether our findings generalize to younger privately insured patients or Medicare beneficiaries enrolled in an HMO. Second, when chemotherapy was provided in a hospital-affiliated outpatient setting, the practice (as measured by the TIN) was not provided on the claims. We were able to determine the practice the physician was associated with by linking the NPI to the MD-PPAS file, which identifies the practice(s) (TIN) that the physician billed to. However, roughly 20% of physicians bill to more than one practice. When this occurred we assigned the physician to the modal TIN (the practice in which they billed most frequently). When examining the proportion of claims billed to the top practice (TIN) for a physician compared to all

others, we found that 80% of their claims were billed to the top practice (TIN). This results in only 4% of claims at risk for misclassification, which should not substantially impact the creation of competition measures. Third, because existing literature has not established a definitive geographic market, we attempted to account for this by creating markets at both the CBSA and HRR levels and found our results were consistent across geographic market definitions.

This study demonstrates that market competition is associated with variation in geographic access to care but does not assess the impact of reduced access to care on patient outcomes, as previous studies have done [15, 21, 51]. Future studies should assess how consolidation and the resulting decreased access to care impacts use of cancer treatments and patient outcomes. Healthcare administrators should consider how acquisitions and mergers may lead to potentially reduced access to care when assessing the potential consequences of consolidation. Although hospitals may improve their financial performance under consolidated delivery systems, this research suggests that patients' access to care may suffer under less competitive markets.

Table 4.1. Sample Characteristic of Fee-for-Service Medicare Cancer Patients Using Chemotherapy Between 2008 and 2014

	All Areas	Urban	Non-Urban
N	142,770	79,172	63,598
Age	75 (7)	75 (7)	75 (7)
Male, %	58%	57%	58%
Race			
White	84%	81%	89%
Black	9%	11%	7%
Other	6%	8%	3%
HHI with CBSA Defined Markets	683 (939)	218 (193)	1,244 (1,152)
HHI with HRR Defined Markets	412 (434)	198 (157)	654 (513)
Number of MDs Providing Chemotherapy			
Within 25 Miles	138 (212)	226 (250)	28 (35)
Within 50 Miles	270 (341)	416 (384)	89 (136)
Within 75 Miles	398 (452)	566 (507)	188 (243)
Distance Travelled			
Mean, SD	100 (252)	87 (239)	117 (267)
Median, IQR	12 (6 - 29)	11 (5 - 23)	15 (7 - 41)
Year			
2008	13%	13%	14%
2009	12%	12%	12%
2010	13%	13%	13%
2011	14%	13%	14%
2012	14%	14%	14%
2013	17%	18%	17%
2014	16%	17%	16%

Note: HHI=Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. HHI is used to measure market completion and is constructed as described in the text. Based on a 20% random sample of Medicare beneficiaries.

Table 4.2. Coefficients of the Association of Log HHI to Distance Traveled to Care

	All	Urban	Non Urban
Distance Travelled to Provider, Fixed Effect Model			
CBSA Market	0.07 (0.06, 0.07)	0.26 (0.25, 0.27)	0.05 (0.04, 0.05)
HRR Market	0.14 (0.13, 0.14)	0.26 (0.25, 0.27)	0.10 (0.10, 0.11)
Sensitivity Analysis: Distance Travelled to Provider, GEE Model			
CBSA Market	0.24 (0.16, 0.31)	0.25 (0.14, 0.37)	0.22 (0.13, 0.31)
HRR Market	0.24 (0.14, 0.34)	0.25 (0.10, 0.40)	0.23 (0.09, 0.36)

Note: Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. GEE=Generalized estimating equations. HHI constructed as described in the text.

Table 4.3. Coefficients of the Association of Log HHI to Number of Chemotherapy Administering Physicians

	All	Urban	Non Urban
Number of Chemotherapy Administering Physicians Within 75 Miles, Fixed Effect Model			
CBSA Market	-0.09 (-0.1, -0.07)	-0.16 (-0.19, -0.13)	-0.07 (-0.09, -0.05)
HRR Market	-0.17 (-0.19, -0.15)	-0.18 (-0.21, -0.15)	-0.17 (-0.19, -0.14)
Sensitivity Analysis: Number of Chemotherapy Administering Physicians Within 75 Miles, GEE Model			
CBSA Market	-0.81 (-0.88, -0.74)	-0.77 (-0.86, -0.68)	-0.87 (-0.97, -0.77)
HRR Market	-0.84 (-0.95, -0.72)	-0.86 (-1.01, -0.71)	-0.80 (-0.97, -0.64)

Note: Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. GEE=Generalized estimating equations. HHI constructed as described in the above text.

Table 4.4. Adjusted Risk Ratios of the Association of Log HHI to Number of Chemotherapy Administering Physicians Within 50 and 25 Miles

	All	Urban	Non Urban
Number of Chemotherapy Administering Physicians Within 50 Miles, Fixed Effect Model			
CBSA Market	-0.16 (-0.17, -0.14)	-0.20 (-0.23, -0.17)	-0.15 (-0.17, -0.13)
HRR Market	-0.23 (-0.25, -0.20)	-0.24 (-0.27, -0.21)	-0.22 (-0.26, -0.19)
Sensitivity Analysis: Number of Chemotherapy Administering Physicians Within 50 Miles, GEE Model			
CBSA Market	-0.90 (-0.95, -0.84)	-0.84 (-0.90, -0.78)	-0.99 (-1.08, -0.90)
HRR Market	-0.87 (-0.98, -0.76)	-0.92 (-1.05, -0.79)	-0.81 (-1.00, -0.61)
Panel B: Number of Chemotherapy Administering Physicians Within 25 Miles, Fixed Effect Model			
CBSA Market	-0.17 (-0.20, -0.15)	-0.26 (-0.31, -0.21)	-0.16 (-0.18, -0.13)
HRR Market	-0.23 (-0.26, -0.20)	-0.27 (-0.32, -0.22)	-0.23 (-0.27, -0.18)
Panel B Sensitivity Analysis: Number of Chemotherapy Administering Physicians Within 25 Miles, GEE Model			
CBSA Market	-0.84 (-0.92, -0.76)	-0.83 (-0.95, -0.72)	-0.85 (-0.93, -0.78)
HRR Market	-0.78 (-0.90, -0.66)	-0.95 (-1.08, -0.81)	-0.50 (-0.68, -0.31)

Note: Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. GEE=Generalized estimating equations. HHI constructed as described in the above text.

CHAPTER 5. EXAMINING THE ASSOCIATION BETWEEN COMPETITION AND SPENDING FOR MEDICARE CANCER PATIENTS

Introduction

Over the past two decades spending on cancer care has dramatically increased, with much of this increase attributed to costly treatments. As the population continues to age, the number of people with cancer requiring treatment will also increase [52, 53]. These two trends, higher cancer care costs and the growing number of people diagnosed and treated for cancer, have particular impact on the Medicare program [53, 54]. Recent analyses suggest that \$1 in \$12 spent on fee-for-service Medicare beneficiaries is spent on cancer care [55]. However, research examining the costs of cancer has focused primarily on technological innovation and patient characteristics with little work examining other factors that can influence the cost of cancer care [53, 56–58].

Mirroring changes happening in the broader healthcare marketplace, the organization of cancer care is changing, with hospitals merging (horizontal integration) and hospitals acquiring physician groups (vertical integration) [12]. Recent research has found that there has been substantial vertical integration in recent years, which has resulted in hospital-owned oncology practices being less than 30% of the market in 2004 to close to 60% in 2015 [12]. Supporters of market consolidation argue that consolidation will result in improved care coordination for patients and improve the quality of care, but critics contend that consolidation will give hospitals disproportionate bargaining power and will result in higher reimbursements for privately insured patients [1, 13]. Although providers cannot directly negotiate to increase their Medicare payments, they can take actions to increase the reimbursable amount they receive from Medicare. First, most hospitals can purchase chemotherapy at deeply discounted prices due to the 340B program [12, 59–61]. Second, hospitals may be able to change an acquired clinic's status from a physician's office to a hospital outpatient department (HOPD) whose Medicare reimbursements are often 50% higher [5, 33, 62]. These factors illuminate the potential

advantages of consolidation to hospitals and clinics. However, there has been little research to examine if reduced market competition in providing chemotherapy infusions has resulted in higher spending for cancer patients. The objective of this study was to examine if reduced market competition is associated with higher spending for similar services.

Methods

Sample

We used a random 20% sample of Medicare fee-for-service claims. We identified new users of infused chemotherapy who were fee-for-service Medicare beneficiaries between 2008 and 2014. To identify a chemotherapy claim, we required that beneficiaries had a cancer-related *International Classification of Disease*, Ninth Edition (ICD-9) code and a Healthcare Common Procedure Coding System (HCPCS) code starting with J9XXX on the same claim. We classified beneficiaries as being a new user of chemotherapy using a six-month wash-out period. Furthermore, we required that beneficiaries were continuously enrolled in Medicare Parts A and B during the wash-out period and for at least six months after initiating chemotherapy (N=86,039). We required the six-month post-chemotherapy follow-up period to examine spending during a “treatment episode” as defined by the Center for Medicare & Medicaid Innovation for the Oncology Care Model [63, 64].

Variables

The primary outcome was total healthcare spending, including payments made by Medicare and the patient (either paid directly by the patient or through supplemental insurance coverage). We measured healthcare spending in three ways. First, we examined the spending for chemotherapy at the line-item level, using only the spending for the HCPCS code for the infused drug. Second, we summed all outpatient spending recorded on the same service day as the drug infusion to capture payments for chemotherapy administration as well as office visits with physicians and other reimbursed services. Third, we examined all healthcare spending (inpatient, outpatient, hospice, durable medical equipment, and home health) starting on the first day of infusion through six months after initiation of chemotherapy, mirroring the chemotherapy

treatment episode as defined by the Center for Medicare & Medicaid Innovation for the Oncology Care Model [63, 64]. All costs were converted to 2014 dollars using the consumer price index.

The main independent variable in our analysis was the competitiveness of a market. We measured competition based on the Herfindahl-Hirschman Index (HHI) [37]. The HHI measures the market structure by squaring the volume shares of a practice within a market. The HHI can range from 0 to 10,000, where the larger the number, the more concentrated and less competitive the market. An HHI of 1,500 or less is considered a competitive market by the federal trade commission. Because it is not clear what constitutes a market for cancer care, we constructed markets at the core-based statistical area (CBSA) and Hospital Referral Region (HRR) level. We used the prevalence cohort of patients and all chemotherapy claims when calculating the HHI to reflect the size of the market. We defined practices (i.e., firms) based on the tax identification number (TIN) listed for the physician administering chemotherapy and their market share as the number of chemotherapy infusions administered by the practice.

We are concerned that practices with high shares are correlated with higher quality practices because patients are more likely to choose higher quality providers. Therefore, because directly measuring market structure may be influenced by unobservable aspects of quality of care, we created an HHI that aims to minimize this bias using the following steps [37, 39, 40]:

1. Create a choice set for patients that will include all practices within 75 miles of a patient's zip code. In sensitivity analysis, we used 25 or 50 miles to test if the results were sensitive to this assumption.
2. Using this choice set, we estimated a patient choice model. Using a conditional logit model, we modeled patient choice as a function of distance between the patient and practice, distance squared, number of physicians associated with the practice (based on the number billing under the TIN), the total annual charges from the practice, charges squared, and year. We included provider size because we believe that patients may prefer larger practices because they are more likely to have had a prior interaction with the facility for other non-cancer-related health care. This model was run

separately for each region (northeast, south, central, and west) to ensure model convergence.

3. We used the estimates from the patient choice model to generate the predicted probability that the patient would use each practice in the patient's choice set. However, the number of physicians and charges of a practice may be associated with the quality of the practice. To overcome this bias, when predicting the probability of visiting a practice we set the number of physicians and charges to the means of that patient's choice set.
4. The predicted probabilities were summed across patients to generate the predicted number of patients that would go to each practice. We calculated the market share for each practice by dividing the number of patients seen at each practice by the number of patients within the market.
5. We then squared each practice's market share and sum the market share across all practices within a market (CBSA or HRR) to generate the level of competition (measured as HHI) for that market.

Because this measure of HHI is purely a function of the geographic distribution of a patient and practices, it does not reflect market share differences due to quality variation across providers. This measure mitigates the causal relationship between market structure and unobservable aspects of quality of care that may otherwise bias our results.

We log HHI, which ensures that both small (i.e., a hospital acquiring a community oncologist) and large (i.e., hospitals merging) changes in HHI will be captured.

Covariates included patients' age, race (black, white, other), gender, year, and an urban indicator (county population > 1 million). We also included fixed effects for the drug used to ensure that any differences seen are not driven by differences in the drugs used but instead by differences in reimbursements for services provided. For the six-month spending models, we included fixed effects for the first chemotherapy drug received.

Statistical Analysis

Generalized linear models were used to assess the relationship between competition and healthcare spending. We used a log link for all models and Poisson distribution for the mean-variance relationship based on the results of the modified Park test. All models controlled for patient characteristics and market area fixed effects (either CBSA or HRR) and the line-item claim and service day models include fixed effects for the drug administered. The market fixed effect provides HHI coefficients that are “within-estimates”—meaning that the HHI coefficient will only be impacted if the competitiveness of a geographic market changes during the study period. These market area fixed effects control for any time invariant factors within a market that could confound the findings, providing a conservative estimate of the impact of competition. Additionally, using fixed effects for the drug administered will ensure that differences seen are not driven by differences in the drugs administered but rather differences in reimbursements for the same services.

Results

Characteristics of the 86,039 individuals included in our cohort are presented in Table 5.1. The mean age of patients was 76 (Standard Deviation (SD):7) and the majority of the population was white (91%). Overall, most patients resided in competitive areas as measured by the HHI(mean is under 1,500). On average, line-item spending on chemotherapy was \$1,973 (SD: \$2,633), service day spending was \$2,196 (SD: \$2,870), and six-month treatment episode spending was \$31,382 (SD: \$29,851).

When considering the role of market competition on healthcare spending we found that competition has small but statistically significant associations at the line and day level but did not have an impact on six-month spending (Figure 5.1). When examining the line-item claim level (Table 5.2), we found that a one standard deviation increase in log HHI (i.e., market becomes less competitive) decreased spending by 1.58 percentage points when markets are created at the CBSA-level (coefficient =-0.07; 95% CI=-0.10, -0.03). The association was larger when measuring markets at the HRR level (coefficient=-0.11; 95% CI=-0.16, -0.06). We saw similar results when measuring healthcare spending at the service day level; we found that a one

standard deviation increase in log HHI is associated with a 1.02 percentage point decrease in healthcare spending when markets were created at the CBSA-level (coefficient=-0.04; 95% CI=-0.07, -0.01). Similarly, the association was larger when measuring markets at the HRR level (coefficient =-0.07; 95% CI=-0.11, -0.03). However, when examining the association of competition on total six-month healthcare spending for a treatment episode (Table 5.2), we did not find a statistically significant association when measuring markets at the CBSA level (coefficient =0.04; 95% CI= -0.01, 0.09) or at the HRR level (coefficient =0.01; 95% CI= -0.04, 0.05).

Discussion

This study documents the association between market competition and spending for chemotherapy services. We found at the chemotherapy claim and day of chemotherapy service level that spending decreased as consolidation increased, however when we looked at six-month total spending by competition level, this difference was no longer statistically significant. This finding was counter to our hypothesis that as a market grew more concentrated spending would increase. Because we controlled for drug received, we know that differences in specific drugs used are not driving the result. Our empirical results show oncology care consolidation only slightly impacted spending at the claim or day level but did not impact overall spending at all.

In this study, we observe spending but not profits from provided services. We believe that one driver of consolidation is to increase positive margins. Hospitals generate positive margins when they purchase independent physician offices because hospitals can purchase chemotherapy at deeply discounted prices through programs such as 340B while being reimbursed at the same or higher rates for chemotherapy by third-party payers. Interestingly, one recent study found that the 340B program was not associated with hospitals buying community practices [12]. If this finding is confirmed by other studies, then it suggests that vertical integration decisions may have been driven by other factors related to payment reform such as Accountable Care Organizations (ACOs) and bundled payments from Medicare as well in attempted response to private insurers increasing use of narrow networks [12].

Our study had several limitations. First, we only included fee-for-service Medicare

beneficiaries and it is unclear if our findings generalize to younger privately insured patients or Medicare beneficiaries enrolled in an HMO. Second, the practice with which a physician was affiliated (as measured by the TIN) was not provided when chemotherapy was provided in a hospital-affiliated outpatient setting. However, we were able to determine the practice the physician was associated with by linking the NPI to the MD-PPAS file, which identifies the practice(s) (TIN) that the physician billed to. It is worth mention that roughly 20% of physicians bill to more than one practice, but when this occurred we assigned the physician to the modal TIN (the practice in which they billed most frequently). Moreover, when examining the proportion of claims billed to the top practice (TIN) for a physician compared to all others, we found that 80% of their claims were billed to the top practice (TIN). This results in a minimal risk of misclassification, with only 4% of claims at risk, which should not substantially impact the creation of competition measures. Third, existing literature has not established a definitive geographic market for chemotherapy. We attempted to account for this by creating two markets definitions, at the CBSA and HRR levels. We found that our results were consistent across geographic market definitions.

These limitations notwithstanding, we present novel findings that increased competition is associated with marginally higher or similar spending on chemotherapy and related services reimbursed by Medicare. This finding was contrary to our initial expectations and may provide comfort to policymakers and regulators who have expressed concerns about consolidation efforts being used solely to increase Medicare reimbursement rates [65]. However, this study is limited to examining how competition impacts spending while competition may also impact patients' access to care, spending for private payers, and the quality of care patients receive. Future research is needed to examine how spending for privately insured patients is impacted by oncology care consolidation to give regulators and policy makers a full picture of the impact of large-scale consolidation.

Table 5.1. Sample Characteristic of Fee-for-Service Medicare Beneficiaries Using Chemotherapy Between 2008 and 2014.

	All Areas
N	86,039
Age	76 (7)
Male, %	60%
Race	
White	91%
Black	6%
Other	3%
Charlson Comorbidity Index	
0	77%
1	12%
2+	11%
HHI with CBSA Defined Markets	441 (433)
HHI with HRR Defined Markets	692 (936)
Line-Item Claim Spending	\$1,973 (\$2,633)
Service Day Spending	\$2,196 (\$2,870)
Six Month Spending	\$31,382 (\$29,851)
Chemotherapy Initiation Year	
2008	14%
2009	13%
2010	14%
2011	14%
2012	15%
2013	20%
2014	10%

Note: All values in parenthesis are standard deviations. HHI=Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. HHI is used to measure market completion and is constructed as described in the above text. Based on a 20% random sample of Medicare beneficiaries.

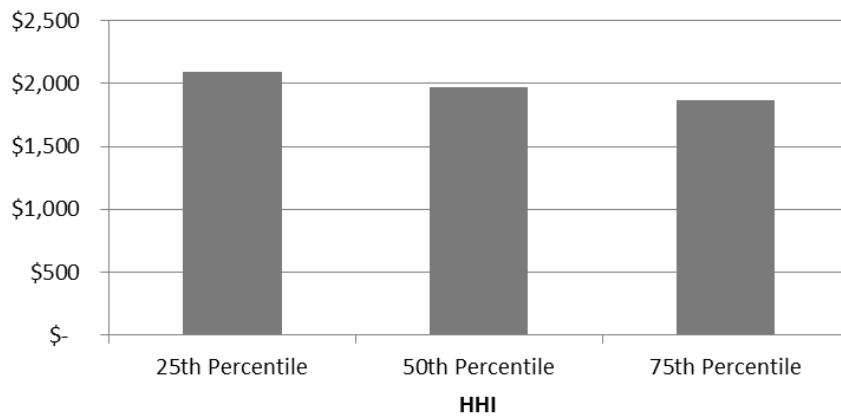
Table 5.2: Coefficients of the Association of Log HHI and Health Care Spending

	Line Item Claim	Service Day	Six Month Episode
CBSA Market	-0.07 (-0.10, -0.03)	-0.04 (-0.07, -0.01)	0.03 (-0.01, 0.07)
HRR Market	-0.11 (-0.16, -0.06)	-0.07 (-0.11, -0.03)	0.04 (-0.01, 0.09)

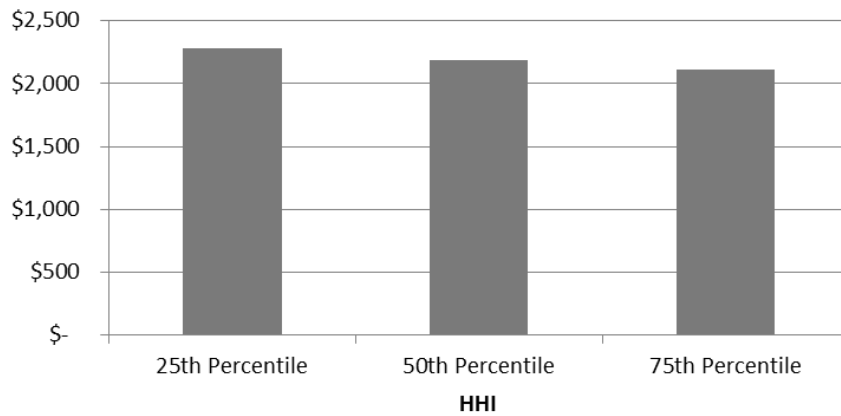
Note: Values in parentheses are 95% confidence intervals. Herfindahl-Hirschman Index; CBSA=core based statistical area; HRR=Hospital referral region. HHI constructed as described in the above text.

Figure 5.1. Predicted Health Care Spending by HHI Quartile

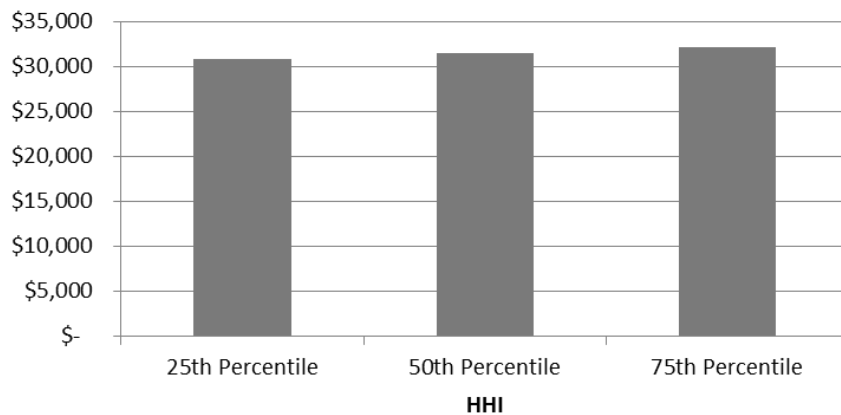
Panel A: Line Item Claim Spending



Panel B: Service Day Spending



Panel C: Six Month Spending



Note: Above estimates based on markets constructed using core-based statistical areas as market areas. HHI=Herfindahl-Hirschman Index

CHAPTER 6. IMPACT OF COMPETITION ON THE USE OF NEW HIGH AND LOW VALUE CHEMOTHERAPY AGENTS

Introduction

The costs of cancer care are staggering [36, 54]. According to the National Cancer Institute, national expenditures for cancer totaled \$124 billion in 2010, and this number is projected to increase more than 25% and reach \$157 billion by 2020.[53] These cost increases have, at least in part, been attributed to use of more new, higher-priced agents [54]. For example, of the 12 FDA-approved cancer drugs in 2012, 11 were priced over \$100,000 per year [66].

High costs of cancer care have created substantial financial burden for patients and payers, leading to increasingly focused discussions around the value of innovation [67–69]. That is, stakeholders are pursuing efforts to measure and understand whether the costs are worth the benefits using cost-effectiveness analysis [69, 70]. Private payers can use these types of value analyses to inform benefit designs to restrict use of low-value drugs among their beneficiaries, but Medicare cannot [71]. Medicare has to provide access to all cancer treatments and has limited ability to control prices or use of low-value treatments [54, 72]. There are few levers that policymakers have to influence the use of low-value treatments for Medicare patients directly. However, one often overlooked approach is to regulate hospital mergers and acquisitions, which is regulated by the Federal Trade Commission as along with some state regulator bodies.

The organization of cancer care is changing, with hospitals merging with other hospitals (horizontal integration) and hospitals acquiring physician groups (vertical integration) [12]. Recent research has found there has been substantial vertical integration, with the percent of oncology practices owned by hospitals nearly doubling (from 30% to nearly 60%) between 2004 and 2015 [12]. There is debate within the health policy community on the impact of consolidation. Supporters argue that consolidation will result in improved care coordination for patients and improve the quality of care, but critics contend that consolidation will result in higher healthcare spending.

One important aspect of quality of care for patients with cancer is the uptake of new high-value treatments or discontinuation of low-value treatments. However, little research has explored how changing competition impacts the diffusion of new treatments [31]. Although fee-for-service Medicare patients will have access to all new cancer treatments under current regulations, prior research has found substantial variation in the diffusion of new high-cost services across hospitals [28, 73, 74] and has found that treatment decisions are often guided by their physicians [75].

The objective of this study is to examine if changes in market competition is associated with the speed of diffusion for new treatments and if the value of treatment modifies the speed of this diffusion.

Methods

Data

To examine the diffusion of new treatments, we considered all intravenously administered chemotherapy agents that were newly approved or previously approved but newly approved for a different indication between 2007 and 2011 (N=15 drugs). We then required at least 5,000 infusions of a specific medication among patients with cancer-related diagnosis codes have sufficient sample size to examine changes over time. This resulted in five candidate drugs for analysis: bevacizumab, nab-paclitaxel, bendamustine, temsirolimus, and degarelix. For each drug, we examined use for a specific indication (bevacizumab/breast cancer; nab-paclitaxel/lung cancer; bendamustine/chronic lymphocytic leukemia (CLL); temsirolimus/kidney cancer; degarelix/prostate cancer).

We categorized drug-indication pairs as high or low value based on an assessment from Memorial Sloan Kettering's Drug Abacus, a recently developed tool that describes the value of a treatment based on price, life expectancy, and side-effect profile. The tool and related value assessment is built on recent work by Howard et al [36].

Sample and Outcome

For each drug/disease pair, we identified a cohort of patients who received any infused chemotherapy with the disease of interest. We also required that patients be continuously

enrolled in Medicare Parts A and B for six months before the infusion to measure comorbidity (breast N=9,499; lung N=4,645; chronic lymphocytic leukemia (CLL) N=2,194; kidney N=1,002; prostate N=22,810). We classified cancer-specific chemotherapy claims based on the *International Classification of Disease*, Ninth Edition (ICD-9) code associated with the line item chemotherapy claim (for any Healthcare Common Procedure Coding System [HCPSC] code beginning with J9XXX). We then summarize a patient's use of treatments at the person-month level. The outcome of interest was use of the drug of interest. Put another way, the numerator is the number of individuals using the drug of interest within a month and the denominator is all patients in the disease cohort that used any chemotherapy within a month.

Exposure

The main independent variable in our analysis was competitiveness of the area. We measured competition based on the Herfindahl-Hirschman Index (HHI). The HHI measures the market structure by squaring volume shares of a practice within a market. We constructed markets at the Hospital Referral Region (HRR) level and conducted sensitivity analyses where markets were constructed at the core-based statistical area (CBSA). We used HRR as the primary analysis because they are large geographic areas that include both urban and rural areas whereas the CBSA fails to include many rural areas. We used a prevalence cohort of all cancer patients and all chemotherapy claims when calculating the HHI. We defined practices based on the tax identification number (TIN) listed for the physician administering chemotherapy and their market share as the number of chemotherapy infusions administered by the practice (see technical appendix for additional information on how physicians were assigned to practices). The HHI can range from 0 to 10,000, where the larger the number, the more concentrated and less competitive the market. An HHI of 1,500 or less is considered a competitive market. We separated HHI into quartiles to allow competition to have a non-linear impact on diffusion and to examine how treatments diffuse in markets with varying levels of competition.

Covariates

For each outcome model we included patients' age, race (white or other), gender, Klabunde adaptation of the Charlson comorbidity score [76], urban indicator (county of residence

population > 1 million), and time. Time was measured as quarter of calendar year since the FDA approval of the medication. If a unique HCPCS was not assigned to the treatment by the time of FDA approval for the indication of interest, we started time once the HCPCS was approved. Additionally, because bevacizumab was approved for use for other indications before 2008, we included the use of bevacizumab in 2007 within a market (CBSA or HRR) for any cancer to account for prior practice patterns.

Statistical Analysis

We summarized baseline characteristics of patients within each disease cohort who received chemotherapy. We then plotted monthly trends in the proportion of patients receiving the treatment of interest among all patients who received chemotherapy for the disease of interest during each month.

To estimate the impact of competition on the diffusion of new medications we used generalized linear models with a log link and binomial distribution and clustered standard errors at the patient level to account for repeated observations. For each disease cohort, we ran separate models. We ran models with and without an interaction between time and HHI quartiles to examine if the slope of the diffusion curve varied. We present adjusted risk ratios (aRR) with 95% confidence intervals (CI) and graphed the predicted probabilities using standardized predictive margins using Stata 10.0 for models with statistically significant associations between HHI and use of the new medication [77].

In June 2010, the FDA communicated that it believed the harms of bevacizumab outweighed the benefits for patients with breast cancer, and prior research has shown that use declined due to this announcement [78]. To account for this event occurring during our study period, for this product we used an interrupted time series analysis to account for the overall time trend in use (time), an indicator variable for the FDA advisory month, and a continuous variable to measure changes in the slope for the “time since” the FDA announcement. We ran models that allow for interactions between HHI quartiles and each of these indicators.

To assess if the value of medications impacted the speed of diffusion, we ran a pooled model of all the drugs included in the analysis (with the exception of bevacizumab since providers

were supposed to stop using it for breast cancer), to measure use of the new treatment. In this analysis, we interacted time and the value of the drug, as defined in the Drug Abacus. We will test if these coefficients are statistically different using a Wald test [79]. Additionally, we interacted value with HHI quartile and tested if they are statistically different.

Sensitivity Analysis

Given that it is not clear what constitutes a market for chemotherapy, we constructed markets at the CBSA level in addition to the HRR market. Results from this sensitivity analysis were consistent with the primary analysis and are not shown.

Results

Across all disease cohorts, we found that the majority of patients receiving chemotherapy are white and roughly half live in urban areas. The average age for patients across cohorts is between 73 and 77. Additionally, we found that patients in the lung and kidney cancer cohorts were more likely to have comorbidities (35.2% and 31.9% with any non-cancer comorbidity) when compared to the CLL, breast, and prostate cancer cohorts (19.9%, 12.8%, 15.6%). We found that roughly half of patients across disease cohorts live in competitive areas (HHI under 1,500).

Diffusion of Medication:

We found that the diffusion of medication varies by treatment (Figure 6.1), with most medications being increasingly used over time.

Nab-Paclitaxel: We find that use of nab-paclitaxel for lung cancer increased from 3.6% of monthly chemotherapy uses in 2012 to 5% in the end of 2014. We find that market competition impacted the diffusion of nab-paclitaxel for patients with lung cancer. When we compared patients in the most competitive markets (quartile 1) to all others we found that patients' use was lower in less competitive markets (quartile 2 vs quartile 1 aRR=0.49, 95% CI=(0.34-0.71); quartile 3 vs quartile 1 aRR=0.60, 95% CI=(0.40-0.90); quartile 4 vs quartile 1 aRR=0.46, 95% CI=(0.31-0.69)). When we examined if the slope of diffusion was impacted by competition by interacting competition with time, one interaction was significant—the interaction between time and the most consolidated quartile increases the use of treatment (aRR=1.12, 95% CI=(1.00, 1.25)). The

graphed predicted probabilities are shown in Figure 6.2 based on the model without an interaction between competition and time.

Bendamustine: We observed that use of bendamustine for CLL increased from 21% in 2008 to 44% of monthly chemotherapy uses in 2014. We found that market competition impacted the diffusion of bendamustine for patients with CLL. When we compared patient in the most competitive markets (quartile 1) to those in the second quartile (aRR=1.34, 95% CI=(1.13, 1.59)) and the most consolidated quartile (aRR=1.28, 95% CI=(1.06-1.54)), we found greater use of the new treatment in less competitive markets. Additionally, when we allowed for interactions between the time and HHI quartiles there were no significant effects. The graphed predicted probabilities are shown in Figure 6.2 based on the model without an interaction between competition and time.

Degarelix: We found that use of degarelix for prostate cancer increased from 1.5% in 2008 to over 14% of monthly chemotherapy uses in 2014. When we examined the association between competition and diffusion of degarelix for men with prostate cancer, we did not find any association with the level of diffusion (quartile 2 vs quartile 1 aRR=1.07, 95% CI=(0.90-1.27); quartile 3 vs quartile 1 aRR=0.94, 95% CI=(0.78-1.13); quartile 4 vs quartile 1 aRR=0.99, 95% CI=(0.73-1.07)). Additionally, when we allowed for interactions between the time and HHI quartiles there were no significant effects.

Temsirolimus: From 2008 to 2014, we found that use of temsirolimus for kidney cancer varied significantly over time from 10% of monthly chemotherapy uses at the end of 2008 to over 50% in the middle of 2009. When examining the association between competition and diffusion of temsirolimus for patients with kidney cancer, we do not find any association with the level of diffusion (quartile 2 vs quartile 1 aRR=1.13, 95% CI=(0.82-1.56); quartile 3 vs quartile 1 aRR=1.09, 95% CI=(0.80-1.49); quartile 4 vs quartile 1 aRR=1.11, 95% CI=(0.81-1.53)). Additionally, when allowing for interactions between the time and HHI quartiles there were no significant effects.

Bevacizumab: From 2008 through 2009, we observed consistent use of bevacizumab for breast cancer at about 6.5% of monthly chemotherapy uses. However, there was a steep decline

to about 2% to 3% of use in 2010 (the time of the FDA announcement) and this steadily declines further to less than 1% in 2012. We did not find any statistically significant associations between market competition and overall level of bevacizumab use.

The Role of Value on Diffusion: When considering the role of value, we find that higher value drugs diffused slower than lower value drugs (aRR=0.96, 95% CI= (0.95-0.97)). However, when testing the relationship of market competition and the value of the medication this did not appear to vary by levels of market competition.

Discussion

Changes in the market structure for cancer care have the potential to impact the use of new treatments [31]. In our sample of Medicare beneficiaries using chemotherapy, use of drugs increased for newly approved treatments between 2008 and 2014. Interestingly, we found that lower value medications diffused faster than higher value medications. However, this finding may be unique to the medications we examined or due to the lack of available alternatives and should be interpreted with caution.

This study found mixed evidence on the influence of competition on the diffusion of new medications. We found that use of nab-paclitaxel and bendamustine was associated with market competition. Nab-paclitaxel, a lower value drug, was used less in concentrated markets whereas the high-value bendamustine was used more in concentrated markets. Looking at these two medications, it may suggest that there is greater centralized control in consolidated markets, which encourages use of higher value medications. However, additional research should be done to examine if this finding is consistent for other medications and in other clinical areas.

Our study had several limitations. First, we only examined fee-for-service Medicare beneficiaries. Therefore, our findings may not be generalizable to younger, privately insured patients or Medicare beneficiaries enrolled in an HMO. Second, when chemotherapy was provided in a hospital-affiliated outpatient setting the practice (as measured by the TIN) was not provided on the claims, however we were able to determine with which practice (TIN) the physician was associated using other files. Because the NPI was recorded for these claims, we were able to link the NPI to the MD-PPAS file, which identifies the practice(s) (TIN) that the

physician billed to. However, for these physicians the MD-PPAS indicates that roughly 20% of physicians bill to more than 1 practice. When this occurred we assigned the physician to the modal TIN (the practice in which they billed most frequently). We found that 80% of their claims were billed to the top practice (TIN) when examining the proportion of claims billed to the top practice (TIN) for a physician compared to all others. This results in only 4% of claims at risk for misclassification, which should not substantially impact the creation of competition measures. Third, because there are no established geographic cancer care markets, we attempted to account for this by creating markets at both the CBSA and HRR levels and found our results were consistent across geographic market definitions.

Little research has explored how provider market structure impacts cancer care [26] and to our knowledge this is the first study that has examined how the market structure impacts the diffusion of new cancer drugs. However, prior studies outside of cancer care that examine how competition impacts diffusion of innovative technologies have found that competitive markets increase the speed of diffusion of a new treatment [27, 29–31]. Our findings demonstrate that competition may impact the use of new treatments, but the impact of competition is modest .

Table 6.1. Sample Characteristics of Fee-For-Service Medicare Beneficiaries Between 2008 and 2014

Cancer of Interest	Lung	CLL	Prostate	Kidney	Breast
Treatment of Interest	Paclitaxel	Bendamistine	Degarelix	Temsirolimus	Bevacizumab
N	4,645	2,194	22,810	1,002	9,499
Age	74.0 (5.8)	76.1 (6.9)	77.5 (7.4)	74.98 (6.57)	73.63 (6.41)
Female, %	49.8%	41.75%	0%	33%	100%
Race					
White	91.5%	93.7%	86.5%	95.1%	90.9%
Black	5.9%	4.8%	10.0%	3.2%	6.6%
Other	2.7%	1.6%	3.5%	1.7%	2.5%
Urban	53.5%	52.4%	52.0%	52.0%	55.2%
Charlson Comorbidity Index					
0	64.8%	80.0%	87.2%	68.1%	84.4%
1	17.9%	9.7%	5.5%	12.5%	9.4%
2+	17.4%	10.3%	7.4%	19.5	6.2%
HHI with HRR Defined Markets	2162 (1767)	2077 (1739)	2004 (1646)	2069 (1710)	2048 (1709)
25 th percentile	850	795	767	899	754
50 th percentile	1488	1540	1398	1603	1448
75 th percentile	2864	2843	2598	3297	2750
Chemotherapy Initiation Year					
2008		16.1%	14.7%	17.4%	14.6%
2009		13.8%	11.2%	15.5%	13.8%
2010		12.9%	14.8%	14.4%	13.2%
2011		15.1%	14.2%	14.5%	14.6%
2012	35.2%	15.0%	14.6%	13.0%	14.8%
2013	44.2%	18.6%	21.0%	16.5%	19.1%
2014	20.6%	8.5%	9.5%	8.9%	9.9%

Note: HHI=Herfindahl-Hirschman Index; HRR=hospital referral regions

Figure 6.1. Diffusion of New Treatments Over Time

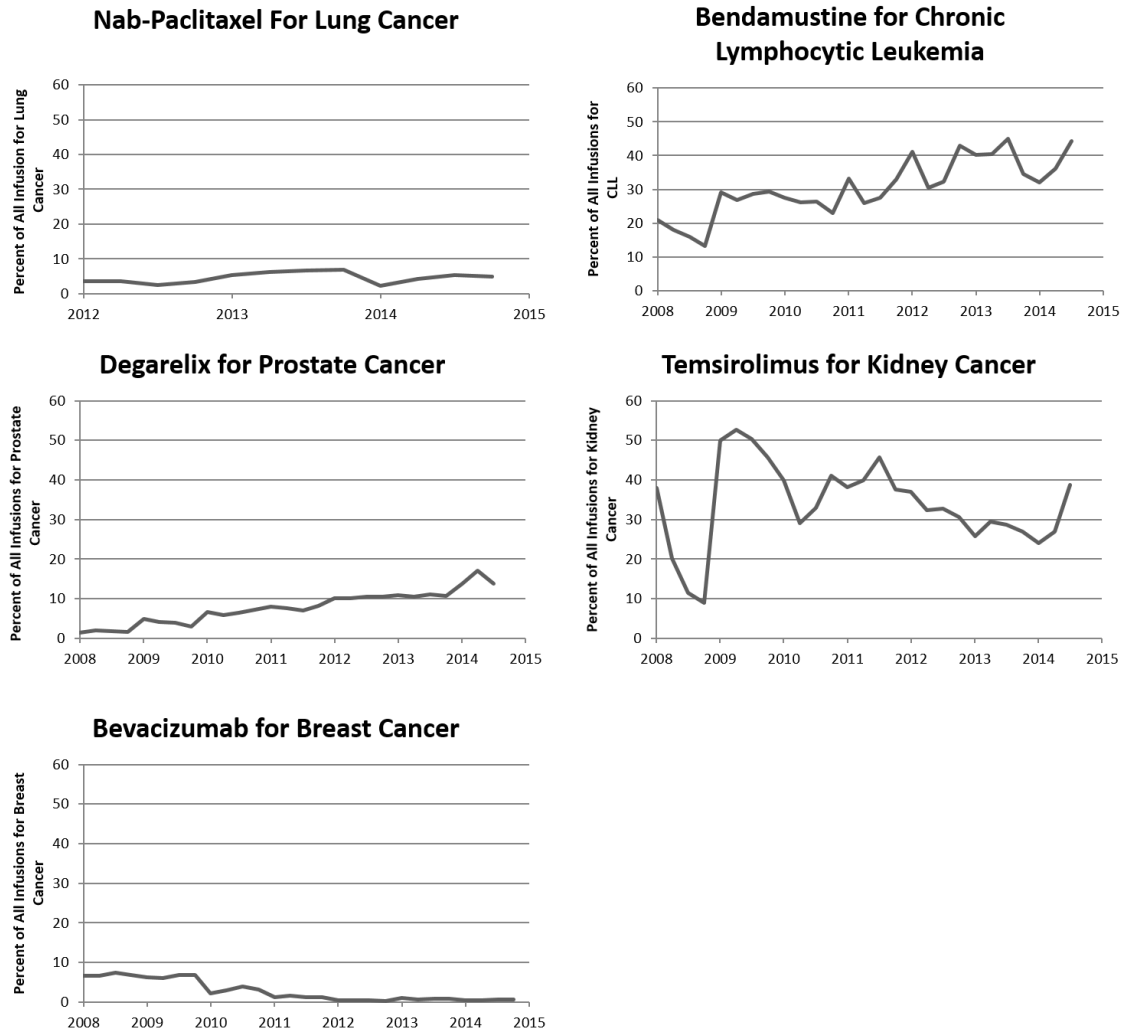
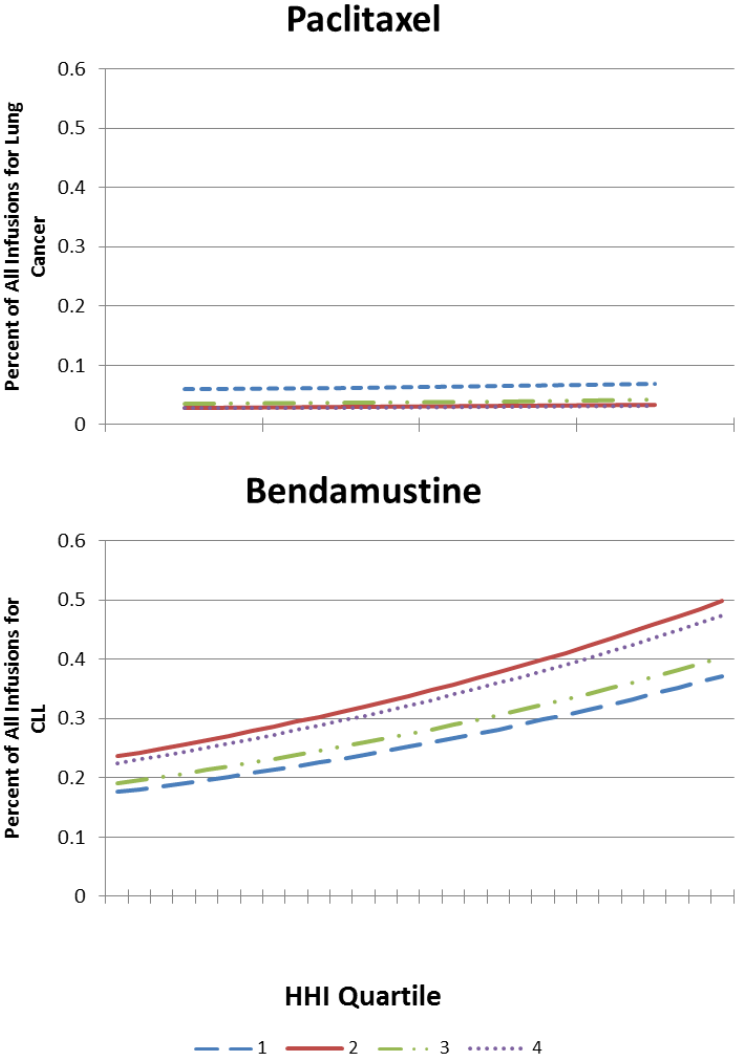


Table 6.2. Adjusted Risk Ratios Showing the Association Between Competition Quartiles and the Use of New Medications

	Paclitaxel		Bendamistine		Degarelix		Temsirolimus	
	Without Interaction	With Interaction	Without Interaction	With Interaction	Without Interaction	With Interaction	Without Interaction	With Interaction
HHI Quartile 1	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
HHI Quartile 2	0.49 (0.34, 0.71)	0.41 (0.20, 0.81)	1.34 (1.13, 1.59)	1.61 (1.13, 2.31)	1.07 (0.90, 1.27)	1.21 (0.79, 1.86)	1.13 (0.82, 1.56)	1.14 (0.65, 2.00)
HHI Quartile 3	0.60 (0.40, 0.90)	0.42 (0.21, 0.84)	1.09 (0.90, 1.31)	1.16 (0.78, 1.73)	0.94 (0.78, 1.13)	1.09 (0.70, 1.70)	1.09 (0.80, 1.49)	1.55 (0.91, 2.63)
HHI Quartile 4	0.46 (0.31, 0.69)	0.22 (0.10, 0.52)	1.28 (1.06, 1.54)	1.15 (0.77, 1.71)	0.88 (0.73, 1.07)	1.17 (0.74, 1.85)	1.11 (0.81, 1.53)	1.20 (0.65, 2.20)
Time	1.05 (1.02, 1.09)	1.01 (0.95, 1.07)	1.03 (1.02, 1.04)	1.03 (1.01, 1.05)	1.07 (1.06, 1.08)	1.08 (1.06, 1.09)	1.00 (0.99, 1.01)	1.01 (0.98, 1.04)
Time*HHI Quartile 1		Reference		Reference		Reference		Reference
Time*HHI Quartile 2		1.03 (0.94, 1.14)		0.99 (0.97, 1.01)		0.99 (0.97, 1.01)		1.00 (0.97, 1.04)
Time*HHI Quartile 3		1.06 (0.97, 1.16)		1.00 (0.97, 1.02)		0.99 (0.97, 1.01)		0.97 (0.94, 1.01)
Time*HHI Quartile 4		1.12 (1.00, 1.25)		1.01 (0.98, 1.03)		0.98 (0.96, 1.01)		0.99 (0.96, 1.03)
Number of Individuals	4645		2194		22810		1002	
Value	Low		High		Marginal		High	

Note: Herfindahl-Hirschman Index; HHI markets are constructed based on hospital referral regions. For each drug, we show the adjusted risk ratios for two models: 1) a simple model that does not allow for interactions and 2) a model that interacts time and quartiles of HHI.

Figure 6.2. Predicted Probabilities for the Diffusion of New Treatments with Statistically Significant Associations with HHI Quartile



Note: HHI=Herfindahl-Hirschman Index

Table 6.3. Adjusted Risk Ratios Showing the Association Between Competition Quartiles and the Diffusion of Bevacizumab

	Use of Bevacizumab
HHI Quartile 1	Reference
HHI Quartile 2	1.42 (0.66, 3.05)
HHI Quartile 3	0.86 (0.37, 1.99)
HHI Quartile 4	1.44 (0.66, 3.17)
Time	0.96 (0.86, 1.08)
Time*HHI Quartile 1	Reference
Time*HHI Quartile 2	1.00 (0.85, 1.17)
Time*HHI Quartile 3	1.11 (0.94, 1.30)
Time*HHI Quartile 4	1.02 (0.87, 1.20)
After Dummy	0.60 (0.23, 1.59)
After Dummy*HHI Quartile 1	Reference
After Dummy*HHI Quartile 2	1.36 (0.35, 5.25)
After Dummy*HHI Quartile 3	0.84 (0.23, 3.05)
After Dummy*HHI Quartile 4	0.37 (0.09, 1.54)
After Time	0.94 (0.81, 1.09)
After Time*HHI Quartile 1	Reference
After Time*HHI Quartile 2	0.90 (0.73, 1.12)
After Time*HHI Quartile 3	0.88 (0.72, 1.08)
After Time*HHI Quartile 4	1.02 (0.83, 1.25)

Note: Herfindahl-Hirschman Index; HHI markets are constructed based on hospital referral regions.

CHAPTER 7. DISCUSSION

Conclusions

Competition and Access to Chemotherapy

Although prior work has documented the impact of geographic access to care for cancer patients, little if any work has explored market factors and their contributions to the geographic distribution of practices. This study aimed to explore the relationship between market competition among oncology providers and patients' geographic access to care. First, we found that most fee-for-service Medicare patients do not travel far for chemotherapy. We observe that 50% of patients travel 12 or fewer miles to receive chemotherapy, with similar median distances travelled between urban and non-urban patients (11 and 15, respectively). However, the top quartile of urban patients travels 23 or more miles while non-urban patients travel 41 miles or more. These results are consistent with prior studies which find that 54% of Stage III colorectal patients travel 12.5 miles or less for adjuvant chemotherapy [15]. Additionally, when examining the number of physicians that provide chemotherapy, we find that non-urban patients have fewer providers within 25 miles, with a mean of only 28 providers compared to 226 for urban patients.

We find that changes in market competition impact geographic access for patients. Our first finding from the adjusted analysis is that as markets become less competitive the distance traveled to chemotherapy increases. Our second finding from the adjusted analysis exploring patient choice found reduced competition is associated with fewer physicians providing chemotherapy close to patients. We test this finding using a variety of sensitivity analyses and find consistent results. These findings suggest that a patient's geographic access to care decreases as markets become less competitive.

Our finding is consistent with news reports where hospital executives justify mergers stating that they will "eliminate duplication—for example by consolidating cardiac care or cancer treatment at one site" [10]. Meaning that hospitals will close some clinical locations to provide

care at a more centralized location in hopes of reduced overhead costs. This will reduce geographic access to care for patients if locations that are shut down are not close to locations that remain open after consolidation occurs.

Our findings are particularly important for patients undergoing chemotherapy treatment, because patients need to repeatedly travel to facilities to receive infused chemotherapy and prior work has found that travel distance can result in reduced adherence to chemotherapy regimens [15]. Additionally this finding is significant because, to our knowledge, it is the first study to examine how geographic access to care is impacted by market competition.

Although our study demonstrates that market competition is associated with variation in geographic access to care, it does not make the leap that variations in geographic access are linked with worse outcomes as previous studies have found [15, 21, 51]. Future studies should assess how consolidation and the resulting decreased access to care impacts use of cancer treatments and patient outcomes. Additionally, healthcare administrators and government regulators should consider how acquisitions and mergers may lead to potentially reduced access when assessing the potential consequences of consolidation as they do when considering how to apply Certificate of Need laws. Although hospitals may improve their financial performance under consolidated delivery systems, this research suggests that patients' access to care may suffer in less competitive markets. Future research can play a role in examining the implications of consolidation for patient access and quality of care.

Competition and Spending

This study documents the association between market competition and spending for chemotherapy services. We found at the chemotherapy claim and day of chemotherapy service level that spending decreased as competition decreased, however when we looked at six-month total spending by competition level, this difference was no longer statistically significant. This finding was counter to our hypothesis that as a market grew more concentrated spending would increase. Because we controlled for drug received, we know that differences in specific drugs used are not driving the result.

In this study, we observe spending but not profit from services. We believe that one driver of consolidation is to increase positive profit margins. Hospitals generate positive margins when they purchase independent physician offices because most hospitals benefit from the 340B program and can purchase chemotherapy at deeply discounted prices while being reimbursed at the same rates. Interestingly, it is not clear that hospitals have been acquiring community oncologists to increase margins due to 340B. A recent study found that the 340B program was not associated with hospitals buying community practices [12]. If this finding is confirmed by other studies, then it suggests that vertical integration decisions may have been driven by other factors related to payment reform such as Accountable Care Organizations (ACOs) and bundled payments from Medicare in attempted response to private insurers' increasing use of narrow networks [12].

We present novel findings that increased competition is associated with marginally higher or similar spending, contrary to our initial expectations. However, this study is limited to examining how competition impacts spending while competition may also impact patients' access to care, spending for private payers, and the quality of care patient receive. Future research is needed to examine how spending for privately insured patients is impacted by oncology care consolidation to give regulators and policy makers a full picture of the impact of large-scale consolidation.

Competition, Value, and the Diffusion of New Treatments

Changes in the market structure for cancer care have the potential to impact the use of new treatments [31]. In our sample of Medicare beneficiaries using chemotherapy, overall we find that use of drugs increased for newly approved treatments between 2008 and 2014. This study found mixed evidence on the influence of competition on the diffusion of new medications. We found that competition was related to differences in diffusion of two of the five treatments studied: nab-paclitaxel and bendamustine. The probability of using nab-paclitaxel (a low-value drug for patients with lung cancer) was lower in less competitive markets whereas the probability of using bendamustine (a high-value drug for patients with CLL) was higher in less competitive markets. Looking at these two medications, it may suggest that there is greater centralized control in

consolidated markets, which encourages use of higher value medications. However, these results were not consistent in three other drug-indication scenarios studied. Additional research should be done to examine if this finding is consistent for other medications and in other clinical areas.

Little research has explored how provider market structure impacts cancer care [26] and to our knowledge this is the first study that has examined how the market structure impacts the diffusion of new cancer drugs. However, from the handful of other studies outside of cancer care that examine how competition impacts diffusion they find that competitive markets increase the speed of diffusion of a new treatment [27, 29–31]. However, the existing literature has not directly explored how the value of a treatment is associated with diffusion. Our findings demonstrate that competition may impact the use of new treatments, but the estimated effect is modest. We also found that lower value medications diffuse slightly faster than high-value medications. This trend is not ideal, however the difference in rates of diffusion was relatively modest. Additionally, research is needed to understand the how the market competition impacts the diffusion of new treatments.

Clinical and Policy Implications

We observed that decreasing competition reduced geographic access to care, reduced spending on chemotherapy, and was somewhat associated with the diffusion of new treatments. Policy makers and hospital administrators should strongly consider how consolidation will impact the geographic access to care for patients and may require that acquiring hospitals assess the expected impact of consolidation on patients' access to care.

When examining the association between spending and competition we find that reduced competition is associated with slightly lower spending for Medicare beneficiaries receiving chemotherapy. This finding should provide comfort to policymakers and regulators who have expressed concerns about consolidation efforts being used solely to increase Medicare reimbursement rates. However, this study provides no information on the impact of consolidation on healthcare spending by private insurers and their patients.

When exploring how new medications have diffused we find a small but inconsistent association with competition. This may suggest that the diffusion of medications is driven by factors other than the competitiveness of a market, such as by patient or physician preference, which suggests that hospital administrators are not strongly directing the use of new medications for Medicare patients. However, this study does not provide a complete picture of the impact of competition on patients and future research should assess how competition impacts patients' use of all types of treatments (chemotherapy, radiation, and surgery) and survival.

Limitations

Our study had several limitations. First, we only examined fee-for-service Medicare beneficiaries. It is unknown whether our findings generalize to younger, privately insured patients or Medicare beneficiaries enrolled in an HMO, however it is likely that geographic access to care will be similar across all patients because almost all providers access to fee-for-service Medicare patients. Second, when chemotherapy was provided in a hospital-affiliated outpatient setting the TIN was not provided on the claims. Therefore, we relied on MD-PPAS to identify the practice the physician was associated with. However, roughly 20% of physicians bill to more than one provider. When this occurred we assigned the physician to the modal practice (the practice in which they billed most frequently). When examining the proportion of claims billed to the top TIN for a physician compared to all others, we found that 80% of their claims were billed to the top TIN. This results in only 4% of claims at risk for misclassification and we believe this did not substantially impact the creation of competition measures. Third, because it is not clear what the proper geographic market is, we attempted to account for this by creating markets at both the CBSA and HRR levels because the existing literature has not established a definitive market area. However, due to the fact that our findings were consistent across definitions, we believe our results will be robust to changing the market definition. Fourth, this study only examines physician-administered medications and fails to examine orally administered anticancer medications.

Future Directions

Understanding how competition impact patients' geographic access to care, spending, and use of new treatments is imperative for informing policy makers and regulators trying to understand and prepare for the rapidly changing healthcare marketplace. The results of this dissertation provide a foundation for future research that:

1. Understands how competition impact patients geographic access to care for other types of treatments (i.e., radiation and surgery) for cancer patients;
2. Explores how patients' adherence to chemotherapy is impacted when the distance to care increases due to consolidation;
3. Explores if the quality volume relationship is consistent with prior research when a consolidation occurs; and
4. Characterizes the type of mergers and acquisitions—are organizations merging in name only or are physicians sharing patients and using similar treatments?

In addition, next steps include several specific research studies to directly extend the results of this dissertation by helping elucidate the type of merger or acquisition. A natural extension of this study could use data that better identifies if a hospital merged with another hospital or purchased a physician group to understand potential heterogeneity in outcomes based on the type of consolidation. Using network analysis, further studies could analytically characterize the type of mergers and acquisitions (i.e., fully integrate physicians into practice, acquired firm's physicians practice independently, etc.) and examine if this drives patient outcomes. Other studies will examine how mergers impact low-income populations and their access to care and outcomes.

REFERENCES

1. Xu T, Wu AW, and Makary MA. The potential hazards of hospital consolidation: Implications for quality, access, and price. *JAMA*. 2015; 314(13): 1337–1338.
2. Cutler DM and Morton FS. Hospitals, market share, and consolidation. *JAMA*. 2013; 310(18): 1964–1970.
3. Moran. *Cost Differences in Cancer Care Across Settings*. 2013. Retrieved from http://www.communityoncology.org/UserFiles/Moran_Cost_Site_Differences_Study_P2.pdf
4. Vandervelde AM, Miller H, and Younts J. *Impact of Medicare Payments of Shift in Site of Care for Chemotherapy Administration*. Berkely, CA: Berkeley Research Group; 2014.
5. MedPAC. *Medicare's Post-Acute Care: Trends and Ways to Rationalize Payments*, in *Report to Congress: Medicare Payment Policy*, M.P.A. Commission, Editor. Washington DC; 2015: 159–177.
6. Baker LC, Bundorf MK, Royalty AB, and Levin Z. Physician practice competition and prices paid by private insurers for office visits. *JAMA*. 2014; 312(16): 1653–1662.
7. Gaynor M. *What do we know about Competition and Quality in Health Care Markets?*, N.B.E.R., Editor. Cambridge, MA; 2006. Retrieved from <http://www.nber.org/papers/w12301>
8. Adler JT, Sethi RK, Yeh H, Markmann JF, and Nguyen LL. Market competition influences renal transplantation risk and outcomes. *Ann Surg*. 2014; 260(3): 550–557.
9. Town RJ, Wholey DR, Feldman RD, and Burns LR. Hospital consolidation and racial/income disparities in health insurance coverage. *Health Aff (Millwood)*. 2007; 26(4): 1170–1180.
10. Pear R. FTC wary of mergers by hospitals, *New York Times*. Sept 18, 2014; 163(56,658):B1.
11. Gaynor M. *Hospital Industry Consolidation*, W.a.M.H. Subcommittee, Editor. Washington DC; 2011.
12. Alpert A, His H, and Jacobson M. Evaluating The role of payment policy in driving vertical integration in the oncology market. *Health Aff (Millwood)*. 2017; 36(4): 680–688.
13. Baicker K and Levy H. Coordination versus competition in health care reform. *N Engl J Med*. 2013; 369(9): 789–791.
14. Baker LC, Bundorf MK, and Kessler DP. Vertical integration: Hospital ownership of physician practices is associated with higher prices and spending. *Health Aff (Millwood)*. 2014; 33(5): 756–763.
15. Lin CC, Bruinooge S, Kirkwood MK, Olsen C, Jemai A, Bajorin D, Giordano SH, Goldstein M, Guadagnolo BA, and Kosty M. Association between geographic access to cancer care, insurance, and receipt of chemotherapy: Geographic distribution of oncologists and travel distance. *J Clin Oncol*. 2015; 33(28): 3177–3185.
16. Wirtz R. *Health care consolidation: Which way is up, and why are we going there?* *FedGazette*. 2015; 9.

17. Dranove D and Lindrooth R. Hospital consolidation and costs: Another look at the evidence. *J Health Econ.* 2003; 22(6): 983–997.
18. Capps C, Dranove D, and Satterthwaite M. Competition and market power in option demand markets. *Rand J Econ.* 2003; 34(4): 737–763.
19. Devers KJ, Casalino LP, Rudell LS, Stoddard JJ, Brewster LR, and Lake TK. Hospitals' negotiating leverage with health plans: how and why has it changed? *Health Serv Res.* 2003; 38(1 Pt 2): 419–446.
20. Gaynor M. Is vertical integration anticompetitive? Definitely maybe (but that's not final). *J Health Econ.* 2006; 25(1): 175–180.
21. Onega T, Duell, EJ, Shi X, Wang D, Demidenko E, and Goodman D. Geographic access to cancer care in the U.S. *Cancer.* 2008; 112(4): 909–918.
22. Celaya MO, Berke EM, Onega TL, Gui J, Riddle BL, Cerala SS, and Rees JR. Breast cancer stage at diagnosis and geographic access to mammography screening (New Hampshire, 1998-2004). *Rural Remote Health.* 2010; 10(2): 1361.
23. Onega T, Duell, EJ, Shi X, Wang D, Demidenko E, and Goodman D. Influence of place of residence in access to specialized cancer care for African Americans. *J Rural Health.* 2010; 26(1): 12–19.
24. Avalere, *Total Cost of Cancer Care by Site of Service: Physician Office vs Outpatient Hospital.* Washington DC: Avalere Health LLC; 2012.
25. Fitch KP and Pyenson B. *Site of Service Cost Differences for Medicare Patients Receiving Chemotherapy.* Washington, D.C.: Milliman; 2011.
26. Carpenter WR, Fortune AK, Zullig LL, and Weiner B. Sustainability and performance of the National Cancer Institute's Community Clinical Oncology Program. *Contemp Clin Trials.* 2012; 33(1): 46–54.
27. Devers KJ, Brewster LR, and Casalino LP. Changes in hospital competitive strategy: a new medical arms race? *Health Serv Res.* 2003; 38(1 Pt 2): 447–469.
28. Bloom BS, Hillman AL, and Schwartz JS. Abruptly changing patterns of diffusion and use of extracorporeal shock-wave renal lithotripsy. *Am J Kidney Dis.* 1991; 18(1): 103–107.
29. Hillman BJ, Winkler JD, Phelps CE, Aroesty J, Williams AP. Adoption and diffusion of a new imaging technology: a magnetic resonance imaging prospective. *AJR Am J Roentgenol.* 1984; 143(4): 913–917.
30. Mohan AV, Fazel R, Huang PH, Shen YC, and Howard D. et al., Changes in geographic variation in the use of percutaneous coronary intervention for stable ischemic heart disease after publication of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial. *Circ Cardiovasc Qual Outcomes.* 2014; 7(1): 125–130.
31. Karaca-Mandic P, Town RJ, and Wilcock A. The Effect of Physician and Hospital Market Structure on Medical Technology Diffusion. *Health Serv Res.* 2017; 52(2): 579–598.
32. Schnipper LE, Davidson NE, Wollins DS, ... and Schilsky RL. American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. *J Clin Oncol.* 2015; 33(23): 2563–2577.

33. Kessler, D. and M. McClellan, *Is Hospital Competition Socially Wasteful?* The Quarterly Journal of Economics, 2000. 115(2): p. 577-615.
34. *HCUP Clinical Classifications Software (CCS) for ICD-9-CM*. . 1/10/2017]; Available from: www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp.
35. Rodriguez RA, Hotchkiss JR, and O'Hare AM. Geographic information systems and chronic kidney disease: racial disparities, rural residence and forecasting. *J Nephrol*. 2013; 26(1): 3–15.
36. Howard D, Bach, PB, Berndt ER, and Conti RM. Pricing in the market for anticancer drugs. *J of Econ Pers*. 2015; 29(1): 139–162.
37. Kessler D and McClellan M. Is hospital competition socially wasteful? *Qtrly J of Econ*. 2000; 115(2): 577–615.
38. Conti R, Landrum MB, and Jacobson M. *The Impact of provider consolidation on outpatient prescription drug-based cancer care spending*. Health Care Cost Institute; Washington DC. 2016.
39. Gozvriskaran G and Town RJ. Competition, payers, and hospital quality. *Health Serv Res*. 2003; 38(6 Pt 1): 1403–1421.
40. Dunn A and Shapiro A. Do physicians possess market power? *J of Law & Econ*. 2014; 57(1): 159–193.
41. Klabunde CN, Potosky AL, Legler JM, and Warren JL. *Development of a comorbidity index using physician claims data*. J Clin Epidemiol, 2000. 53(12): p. 1258-67.
42. Baldwin LM, Cai Y, Larson EH, Dobie SA, Wright GE, Goodman DC, Matthews B, and Hart LG. Access to cancer services for rural colorectal cancer patients. *J Rural Health*. 2008; 24(4): 390–399.
43. Chan L, Hart LG, and Goodman DC. Geographic access to health care for rural Medicare beneficiaries. *J Rural Health*. 2006; 22(2): 140–146.
44. Probst JC, Laditka SB, Wang JY, and Johnson AO. Effects of residence and race on burden of travel for care: cross sectional analysis of the 2001 US National Household Travel Survey. *BMC Health Serv Res*. 2007; 7: 40.
45. Kirkwood MK, Bruinooge SS, Goldstein MA, Bajorin DF, and Kosty MP. Enhancing the American Society of Clinical Oncology workforce information system with geographic distribution of oncologists and comparison of data sources for the number of practicing oncologists. *J Oncol Pract*. 2014; 10(1): 32–38.
46. Ananthakrishnan AN, Hoffmann RG, and Saeian K. Higher physician density is associated with lower incidence of late-stage colorectal cancer. *J Gen Intern Med*. 2010; 25(11): 1164–1171.
47. Ferrante JM, Gonzalez EC, Pal N, and Roetzheim RG. Effects of physician supply on early detection of breast cancer. *J Am Board Fam Pract*. 2000; 13(6): 408–414.
48. Fleisher JM, Lou JQ, and Farrell M. Relationship between physician supply and breast cancer survival: a geographic approach. *J Community Health*. 2008; 33(4): 179–182.
49. Schroen AT, Brenin DR, Kelly MD, Knaus WA, and Slingluff CL Jr. Impact of patient distance to radiation therapy on mastectomy use in early-stage breast cancer patients. *J Clin Oncol*. 2005; 23(28): 7074–7080.

50. Glick H, Doshi JA, and Sonnad SS. Economic evaluation in clinical trials. In *Handbooks in Health Economic Evaluation*. Second ed. Oxford, UK: Oxford University Press; 2015; x, 252.
51. Ahamad A. Geographic access to cancer care: A disparity and a solution. *Postgrad Med J*. 2011; 87(1031): 585–589.
52. Bureau UC. *Interim Projections Consistent With Census 2000*, P. Division, Editor. Washington DC; 2004.
53. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, and Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. *J Natl Cancer Inst*. 2011; 103(2): 117–128.
54. Bach PB. Limits on Medicare's ability to control rising spending on cancer drugs. *N Engl J Med*. 2009; 360(6): 626–633.
55. Maroongroge S, Kim SP, Mougalian S, ... and Yu JB. et al., The cost of cancer-related physician services to Medicare. *Yale J Biol Med*. 2015; 88(2): 107–114.
56. Farina KL. The economics of cancer care in the United States. *Am J Manag Care*. 2012; 18(1 Spec No.): SP38–39.
57. Schrag D. The price tag on progress—Chemotherapy for colorectal cancer. *N Engl J Med*. 2004; 351(4): 317–319.
58. Mariotto AB, Yabroff KR, Feuer EJ, De Angelis R, and Brown M. Projecting the number of patients with colorectal carcinoma by phases of care in the US: 2000–2020. *Cancer Causes Control*. 2006; 17(10): 1215–1226.
59. Clark BL, Hou J, Chou CH, Huang ES, and Conti R. The 340B discount program: outpatient prescription dispensing patterns through contract pharmacies in 2012. *Health Aff (Millwood)*. 2014; 33(11): 2012–2017.
60. Conti RM and Bach PB. The 340B drug discount program: hospitals generate profits by expanding to reach more affluent communities. *Health Aff (Millwood)*. 2014; 33(10): 1786–1792.
61. Conti RM and Bach PB. Cost consequences of the 340B drug discount program. *JAMA*. 2013; 309(19): 1995–1996.
62. Grant DS, Stewart J, Samchok D, Arnold C, Godfrey E, and Legomsky J. *CMS is Taking Steps to Improve Oversight of Provider-Based Facilities But Vulnerabilities Remain*, H.a.H. Services, Editor. Washington DC: Office of the Inspector General; 2016.
63. *Oncology Care Model—OCM Performance-Based Payment Methodology*. Washington DC: Centers for Medicare and Medicaid Services; 2016.
64. CMMI, *Oncology Care Model (OCM) Request for Applications*, C.f.M.a.M. Innovation, Editor. Washington DC: Centers for Medicare and Medicaid Services; 2015.
65. Higgins AV and Veselovskiv G. *Does The Site Of Care Change The Cost Of Care?* Health Affairs; 2016. Retrieved from <http://healthaffairs.org/blog/2016/06/02/does-the-site-of-care-change-the-cost-of-care>
66. Abboud C, Berman E, Cohen A, ... and Salem Z. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: From the perspective of a large group of CML experts. *Blood*. 2013; 121(22): 4439–4442.

67. Schnipper LE, Davidson NE, Wollins DS, ... and Schilsky RL. American Society of Clinical Oncology statement: A conceptual framework to assess the value of cancer treatment options. *J Clin Oncol*. 2015; 33(23): 2563–2577.
68. Cavallo J. Calculating the value of cancer drugs. *ASCO Post*. 2015; 6(15).
69. Winn AN, Ekwueme DU, Guy GP Jr., and Neumann PJ. Cost-utility analysis of cancer prevention, treatment, and control: A systematic review. *Am J Prev Med*. 2016; 50(2): 241–248.
70. Greenberg D, Earle C, Fang CH, Eldar-Lissai A, and Neumann PJ. When is cancer care cost-effective? A systematic overview of cost-utility analyses in oncology. *J Natl Cancer Inst*. 2010; 102(2): 82–88.
71. Chambers JD, Cangelosi MJ, and Neumann PJ. Medicare's use of cost-effectiveness analysis for prevention (but not for treatment). *Health Policy*. 2015; 119(2): 156–163.
72. Chambers JD and Neumann PJ. Listening to Provenge--what a costly cancer treatment says about future Medicare policy. *N Engl J Med*. 2011; 364(18): 1687–1689.
73. Fendrick AM, Escarce JJ, McLane C, Shea JA, and Schwartz JS. Hospital adoption of laparoscopic cholecystectomy. *Med Care*. 1994; 32(10): 1058–1063.
74. Banta HD. The diffusion of the computed tomography (CT) scanner in the United States. *Int J Health Serv*. 1980; 10(2): 251–269.
75. Puts MT, Tapscott B, Fitch M, ... and Alibhai SM. A systematic review of factors influencing older adults' decision to accept or decline cancer treatment. *Cancer Treat Rev*. 2015; 41(2): 197–215.
76. Klabunde CN, Legler JM, Warren JL, Baldwin LM, and Schrag D. A refined comorbidity measurement algorithm for claims-based studies of breast, prostate, colorectal, and lung cancer patients. *Ann Epidemiol*. 2007; 17(8): 584–590.
77. Williams R. Using the margins command to estimate and interpret adjusted predictions and marginal effects. *Stata Journal*. 2012; 12(2): 308–331.
78. Dusetzina SB, Ellis S, Freedman RA, ... and Keating NL. How do payers respond to regulatory actions? The case of bevacizumab. *J Oncol Pract*. 2015; 11(4): 313–318.
79. Cameron AC and Trivedi PK. *Microeconometrics: Methods and Applications*. New York: Cambridge University Press, 2005; xxii, 1034.